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Can immature granulocyte count be a new biomarker for the evaluation of inflammation in patients with obstructive sleep apnea syndrome? A single-centre study

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Abstract

Background & Objective: Obstructive sleep apnea syndrome (OSAS) is the most common sleep-related breathing disorder. The potential use of the immature granulocyte count as an inflammation marker in certain diseases has been investigated. This study aims to investigate the feasibility of using haemogram parameters including immature granulocyte levels as an inflammatory marker in patients with OSAS and the relationship between this parameter and disease severity. *Methods:* This retrospective study was conducted using the data of 101 OSAS patients and 114 healthy controls. Demographic and polysomnographic data were recorded in the OSAS group. The OSAS patients were subdivided into three sub-groups according to apnea-hypopnea index. Haemogram parameters, white blood cell count (WBC), neutrophil/lymphocyte ratio (NLR), haemoglobin (HGB), haematocrit (HCT), lymphocyte count, mean platelet volume (MPV), platelet count (PLT), MPV/PLT ratio, PLT/lymphocyte ratio (PLR), WBC/MPV ratio (WMR), IGc and IG percentage (IG%) values were compared between the OSAS and control groups. *Results:* Haemogram parameters WBC, HGB, HCT, IGc and IG%, lymphocyte count and WMR values were found to be statistically significantly higher and PLR value was lower in the OSAS group. In OSAS subgroups, only HGB and HCT values were found to be significantly higher, parallel to disease severity. As a result of the ROC analysis between the control and OSAS groups, it was determined that the HCT, WBC, PLR, IGc and IG%, lymphocyte count and WMR values had a significant value in presenting increased inflammation in OSAS.
Conclusion: IGc may be used as a novel parameter to indicate increased inflammation in OSAS patients.

Keywords: Sleep apnea, ımmature granulocyte, ınflammatıon

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent partial/complete collapse of the upper respiratory airway, resulting intermittent hypoxemia during sleep.[1] Among middle-aged adults, about 4% of men and 2% of women are affected.[1] The main pathophysiological and etiologic mechanisms are still unknown but chronic inflammation, is one of the key pathological mechanisms in the course of OSAS.[2] Although not yet fully elucidated, it is thought that recurrent short-term hypoxia activates numerous inflammatory pathways. From another perspective, inflammation may also be one of the underlying factors contributing to upper airway obstruction in OSAS.[3] The thickening of the lateral pharyngeal wall, which leads to obstruction, has been shown to be primarily due to soft tissue swelling, which has been interpreted as possibly being triggered by inflammation.[2,3]

In a study evaluating the histopathological findings of pharyngeal tissue, patients with OSAS exhibited significantly more widespread edema, vasodilation, and mucous gland hypertrophy compared to controls.[4] These findings suggest that inflammation plays a significant role in upper

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airway narrowing and may contribute to a vicious cycle by exacerbating OSAS severity.

The immature granulocyte (IG) fraction in peripheral blood is a parameter that is poorly recognised by most clinicians. The IG count (IGc), an indicator of local and systemic inflammation, can be measured using the complete blood count (CBC). In recent years, it has been shown to be useful in predicting the severity and mortality of many diseases such as acute pancreatitis, sepsis and cancer.[5-7]

In this study, we aimed to evaluate the effectiveness of hemogram parameters, including IGc, in indicating increased inflammation in OSAS patients and to investigate the potential relationship between these parameters and disease severity.

METHODS

Data collection

This retrospective study included 101 patients between ages 24 and 68 who had undergone polysomnography examination at the sleep laboratory of the neurology department in Mazhar Osman Educational and Research Hospital, Turkey between January 2021 and October 2023 and 114 healthy controls with age and gender compatibility. The medical history and clinical characteristics of all participants were recorded, and body mass index (BMI) was calculated as weight (kg)/height^2 (m^2) in OSAS patients.

Patients with the following characteristics were not included in the study: age under 18 years; current pregnancy; myeloproliferative disease; chronic inflammatory, liver or kidney disease; chronic obstructive pulmonary disease, asthma; psychiatric causes of sleep disorders, central sleep apnea, narcolepsy; chronic alcoholism; use of sedatives or muscle relaxants; malignancy; use of granulocyte colony-stimulating factor, immunosuppressive agent or steroid; use of antithrombotic, anticoagulant or antiepileptic drugs; existence of uncontrolled hypertension (blood pressure>140/90 mm Hg under medical treatment), hyperlipidemia (low-density lipoprotein cholesterol (LDL-C) level of ≥140 mg/dL) or diabetes (HBA1c level of >8% under medical agents) ; acute inflammation, infection. Fasting blood samples were taken from peripheral venous blood. Recorded parameters were platelet (PLT) and lymphocyte count, haemoglobin (HGB), haematocrit (HCT), IGc and Ig %, mean platelet volume (MPV); calculated values included neutrophil/lymphocyte ratio (NLR), PLT/lymphocyte ratio (PLR) and MPV/PLT, white blood cell/MPV (WBC/MPV) ratio (WMR). All haemogram parameters were calculated using an automated blood analyzer (Hematologic Analyzer, Beckman Coulter Inc., Brea CA USA). Our study was conducted in accordance with the Helsinki Declaration, upon approval from the local ethics committee (decision date: November 06, 2023; number: 21/05). All participants were voluntary, were informed about the study and gave written consent.

Polysomnography (PSG) examinations at the sleep laboratory were conducted before inclusion in this study. Full-night attended polysomnograms included six-channel electroencephalography, two-channel electrooculography, submental and left/right anterior tibial electromyography (EMG), electrocardiography, breath sound recording, oro-nasal thermal sensor, nasal pressure sensor, body position probe, thoracal and abdominal sensors, pulse oximeter and synchronous video recordings. Wake-sleep patterns and sleep-related abnormal breathing events were scored using the 2020 criteria of American Academy of Sleep Medicine (AASM).[8] PSG recordings of OSAS subjects were scored by a sleep expert who was blinded to blood test results. Additional parameters evaluated in OSAS patients were minimum oxygen saturation, mean oxygen saturation, desaturation index, apnea-hypopnea index (AHI), total sleep time (TST) and mean heart rate.

The patients diagnosed with OSAS were divided into three groups: Group 1 (mild OSAS): AHI 5-14 times/hour, n = 33, Group 2 (moderate OSAS): AHI 15–29 times/hour, n = 30, Group 3 (severe OSAS): AHI ≥ 30 times/hour, n = 38.

Statistical analyses were performed using SPSS Statistics for Windows, version 25 (SPSS Inc., Chicago, IL, USA). Frequency and percentage values are presented for qualitative variables. Quantitative variables with normal distribution are expressed as mean ± standard deviation (SD) while median, minimum and maximum values are presented for variables that do not comply with normal distribution. Normality of distribution was examined using the Shapiro-Wilk test. Chi-square test was used for comparisons between two qualitative variables. In comparisons between two-category qualitative variables and quantitative variables, the independent sample t-test was used if the data conformed to normal distribution, and the Mann-Whitney U test was used if the data did not conform to normal distribution. In comparisons between qualitative variables

with more than two categories and quantitative variables, one-way ANOVA was used if the data conformed to normal distribution, and the Kruskal-Wallis H test was used if the data did not conform to normal distribution. If there was a significant difference as a result of one-way ANOVA, categories were determined using the Tukey test; if there was a significant difference as a result of the Kruskal-Wallis H tests, the categories were compared in pairs using the Mann-Whitney U test. The ability of biomarkers to distinguish patients with OSAS was examined using ROC analysis. The existence of a relationship between two quantitative variables was examined with Spearman correlation. In all analyses, p<0.05 was accepted as statistically significant.

RESULTS

A total of 215 cases, 101 OSAS patients and 114 healthy controls, were included in the study. Table I summarizes the descriptive and laboratory statistics of the variables compared between OSAS patients and the control group. As seen in Table 1, there was no significant difference among the OSAS groups in terms of their median age (p = 0.371) or gender (p = 0.801). The differences among the OSAS patients and control group, based on the HGB, HCT, WBC, IGc and IG%, lymphocyte and PLR and WMR values, were significant (p<0.05). All of these values except PLR were higher in OSAS patients compared to controls (Table 1).

In ROC curve analysis of laboratory parameters of patients with OSAS, HCT (p = 0.014; AUC = 0.597), WBC (p = 0.005; AUC = 0.609), PLR (p = 0.003; AUC = 0.614), IGc (p = 0.004; AUC = 0.608), IG% (p = 0.009; AUC = 0.598), lymphocyte count (p = 0.001; AUC = 0.632) and WMR (p = 0.041; AUC = 0.58) markers were found to be significant. HGB (p = 0.053), platelet (p = 0.652), MPV (p = 0.406), NLR (p

Table 1: Demographic and laboratory results in OSAS and control groups

	Control group n (%)	**OSAS group n (%)**	**Total n (%)**	**Chi-square**	**p**
Female	41 (36)	38 (37,6)	79 (36,7)	0,063	0,801
Male	73 (64)	63 (62,4)	136 (63,3)		
	Control group Med (min-max) / $\bar{x}$ ± SS	**OSAS group Med (min-max) / $\bar{x}$ ± SS**	**Total Med (min-max) / $\bar{x}$ ± SS**	**t/Z**	
Age	47,5 (36-69)	48 (24-68)	48 (24-69)	-0,895^{Z}	0,371
HGB	13,8±1,53	14,27±1,6	14,02±1,58	-2,198^{t}	**0,029***
HCT	42,05 (30,5-48,3)	43,7 (33,4-52,5)	42,5 (30,5-52,5)	-2,46^{Z}	**0,014***
WBC	6,73 (3,39-10,87)	7,3 (4,06-10,88)	7,08 (3,39-10,88)	-2,757^{Z}	**0,006***
Platelet	249,5 (148-423)	246 (147-474)	248 (147-474)	-0,453^{Z}	0,651
MPV	10,16±1,26	10,27±1,09	10,21±1,18	-0,704^{t}	0,482
NLR	1,91 (0,83-5,53)	1,7 (0,73-5,54)	1,83 (0,73-5,54)	-1,327^{Z}	0,185
MPV/PLT	0,04 (0,02-0,08)	0,04 (0,02-0,09)	0,04 (0,02-0,09)	-0,194^{Z}	0,846
PLR	118,74 (52,6-291,38)	103,35 (49,12-212,22)	112,38 (49,12-291,38)	-2,873^{Z}	**0,004***
IGcount	0,01 (0-0,1)	0,02 (0-0,9)	0,01 (0-0,9)	-2,82^{Z}	**0,005***
IGpercent	0,2 (0-0,9)	0,2 (0,1-1,1)	0,2 (0-1,1)	-2,525^{Z}	**0,012***
Plateletcrit	0,25 (0,15-0,4)	0,25 (0,17-0,46)	0,25 (0,15-0,46)	-0,422^{Z}	0,673
RDWCV	13,5 (12,1-16,4)	13,4 (11,8-16)	13,4 (11,8-16,4)	-0,783^{Z}	0,434
Lymphocyte	2,12 (0,58-3,84)	2,42 (0,82-5,7)	2,22 (0,58-5,7)	-3,348^{Z}	**0,001***
Neutrophil	3,88 (1,9-9,34)	4,3 (2,24-9,31)	4,12 (1,9-9,34)	-1,744^{Z}	0,081
WMR	0,68 (0,27-1,28)	0,76 (0,36-1,35)	0,71 (0,27-1,35)	-1,987^{Z}	**0,047***

*p<0,05 | ^{t}: Independent Sample T test | ^{Z}: Mann-Whitney U test

= 0.186), MPV/PLT (p = 0.544), plateletcrit (p = 0.675), RDWCV (p = 0.433) and neutrophil count (p = 0.078) markers could not be used to distinguish between healthy individuals and patients with OSAS (Table 2). As a result of the assessment made by the ROC curve analysis, it was determined that the HCT, WBC, PLR, IGc, lymphocyte count and WMR values can be alternative inflammation markers in OSAS. The ROC curves are shown in Figure 1.

The descriptive, polysomnography and laboratory values of OSAS patients are summarized in (Table 3). There was no significant difference in the OSAS groups in terms of their mean age, sex, BMI, TST, mean oxygen saturation, sleep efficiency and mean heart rate values (p>0.05). The differences among the OSAS groups based on the minimum O_2 saturation and desaturation index values were significant (p<0.05). As the severity of OSAS changed from mild to severe, the min O_2 saturation values decreased and desaturation index values increased. In the laboratory tests, the difference among the OSAS groups was significant in terms of the HGB and HCT (p<0.05), which increased as the AHI score increased. As the severity of OSAS changed from mild to severe, the lymphocyte and IGc values increased, but differences among the OSAS groups in terms of those parameters were insignificant (p>0.05). The differences among the OSAS groups in terms of the WMR, PLR and NLR values were not significant (p>0.05) (Table 3).

As a result of the correlation analysis between AHI values and other variables, it was determined that there was a weak positive relationship between AHI and BMI (p = 0.009; r = 0.259), HGB (p<0.001; r = 0.365) and HCT (p<0.001; r = 0.371) values. There was a moderate negative relationship between AHI and min O_2 saturation (p<0.001; r = -0.558) and a weak negative relationship between AHI and mean O_2 saturation (p = 0.023; r = -0.227) and PLR (p = 0.008; r = -0.264). There was a positive relationship between AHI and desaturation index values (p<0.001; r = 0.958). There was no significant relationship between AHI and age (p = 0.578), TST (p = 0.887), sleep efficiency (p = 0.957), mean heart rate (p = 0.127), WBC (p = 0.175), platelet (p = 0.227), MPV (p). =0.769), NLR (p = 0.178), MPV/PLT (p = 0.335), IGc (p = 0.401), IG% (p = 0.08), plateletcrit (p = 0.244), RDWCV (p = 0.500), lymphocyte count (p = 0.198), neutrophil count (p = 0.551) or WMR (p = 0.159) values (Table 4).

DISCUSSION

Although the underlying pathophysiology of OSAS is not completely understood; hypoxia, chronic intermittent inflammation and/or increased sympathetic activity have been proposed as the most significant mechanisms.[9] Chronic

Table 2: Laboratory markers in OSAS patients

	AUC	95% CI	SE	p	Cut-off	Sens	Spes
HGB	0,576	0,507-0,643	0,0394	0,053	>14,7	45,54	72,81
HCT	0,597	0,528-0,663	0,0394	**0,014***	>44,5	47,52	76,32
WBC	0,609	0,540-0,675	0,0384	**0,005***	>6,27	80,20	41,23
Platelet	0,518	0,449-0,586	0,0397	0,652	>308	24,75	83,33
MPV	0,533	0,464-0,601	0,0394	0,406	>9,7	67,33	41,23
NLR	0,552	0,483-0,620	0,0394	0,186	≤1,75	55,45	60,53
MPV/PLT	0,523	0,454-0,592	0,0382	0,544	≤0,05	87,13	17,54
PLR	0,614	0,545-0,679	0,0384	**0,003***	≤104,11	53,47	66,67
IGcount	0,608	0,538-0,674	0,0368	**0,004***	>0,01	55,67	60,53
IGpercent	0,598	0,529-0,665	0,0378	**0,009***	>0,1	74,23	43,86
Plateletcrit	0,517	0,448-0,585	0,0397	0,675	>0,35	12,87	94,74
RDWCV	0,531	0,462-0,599	0,0394	0,433	≤14,3	91,09	23,68
Lymphocyte	0,632	0,564-0,697	0,0379	**0,001***	>2,29	59,41	65,79
Neutrophil	0,569	0,500-0,636	0,0391	0,078	>3,92	62,38	52,63
WMR	0,580	0,511-0,647	0,0391	**0,041***	>0,74	53,47	62,28

Abbreviations: AUC: Area under the curve; SE: Standard Error; CI: Confidence Interval. HGB: Hemoglobin, HCT: Hematocrit, WBC: White Blood Cell; MPV: Mean Platelet Volume; RDW: Red Cell Distribution Width; NLR: Neutrophil to Lymphocyte Ratio, PLR: Platelet to Lymphocyte Ratio, WMR: White Blood Cell to Mean Platelet Volume Ratio

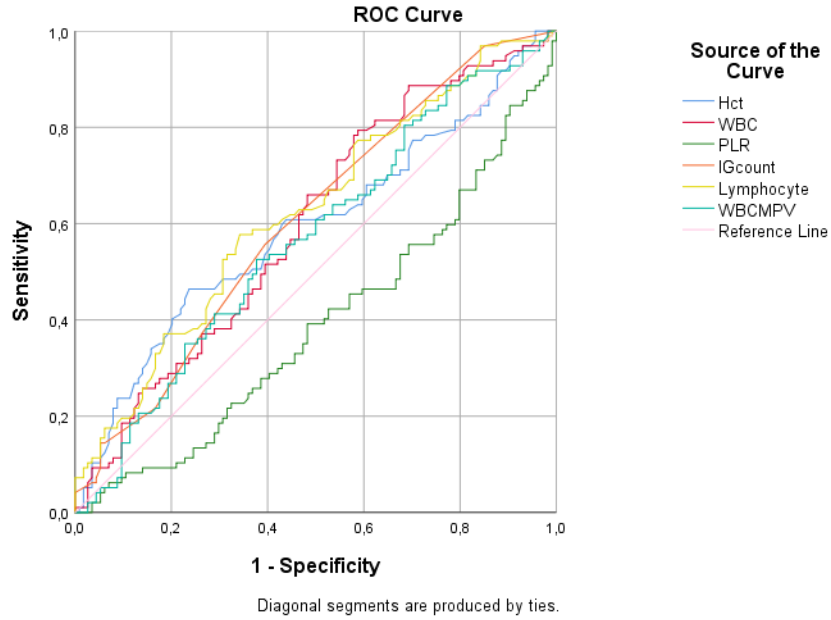

Figure I: Receiver operating characteristic curves for inflammatory markers in diagnosis of OSAS

systematic inflammation has a significant role in determining prognosis of OSAS.[10]

Determination of inflammatory markers in assessing the degree of nocturnal hypoxia and predicting the presence of complications in OSAS patients is important. OSAS is associated with complications such as cardiovascular, malignant or metabolic.[11] Generally, haematological parameters in CBC, which are simple and inexpensive, are frequently used to measure the inflammatory status in daily clinical practice.[9] Various proinflammatory cytokines (e.g., TNF-a, VEGF, interleukin-1 (IL-1) and IL-6) are secreted in inflammation.[1] Some biomarkers, such as tumour necrosis factor (TNF-a), VEGF, IL-1 and IL-6 are expensive to measure in routine use. Clinical measurement of the inflammatory status needs new specific biochemical markers.

It is thought that hypoxia and fragmentation during sleep leading to sympathetic discharges which trigger inflammation and activate platelet aggregation and adhesion.[12] Induced platelet production results in increased MPV values.[13,14] While some studies similar to our study showed no difference in MPV values between control and OSAS patients.[4,14] Others reported increased MPV values in patients with severe OSAS.[2,15,16] In our study MPV value was higher in the OSAS group compared to the control group, and higher in severe OSAS than in mild and moderate subgroups, but without a statistically significant difference. These different study results may be related to the presence of acute or chronic hypoxia.[12,15,16]

Because high platelet count is associated with inflammation and low lymphocyte levels are related to uncontrolled inflammatory pathways, PLR may be a useful biomarker in inflammation.[17,18] Several studies indicate that PLR and NLR might predict OSAS severity[19-21], but in another study, the NLR and PLR levels did not increase as the severity of OSAS increased.[13] Some researchers have observed elevated[21,22] whereas some others have found decreased NLRs levels[3,24-26] in patients with OSAS compared to controls. When comparing OSAS patients to controls in terms of NLR values, no statistically significant difference was found ($p = 0.611$), but a statistically significant relationship between decreased PLR value and OSAS severity was found ($p = 0.019$).[3] Another study found a high NLR in patients with OSAS, correlated with AHI, and concluded that NLR≥1.62 is an independent biomarker for OSAS.[22] In our study we found decreased NLR and PLR values in OSAS patients comparing to healthy controls similar to some articles in the literature.[3,24,25]

Although NLR and PLR levels are considered an indication of increased systemic inflammation, in our study NLR values decreased in parallel with the severity of OSAS but was not at a statistically significant level. The difference and incongruity of

Table 3: Polysomnography variables and laboratory results in OSAS sub-groups

	MILD OSAS (A) n:33 Med (min-max) / $\bar{x}$ ± SD	MODERATE OSAS (B) n:30 Med (min-max) / $\bar{x}$ ± SD	SEVERE OSAS (C) n:38 Med (min-max) / $\bar{x}$ ± SD	Total OSAS n:101 Med (min-max) / $\bar{x}$ ± SD	F/H	p	Difference
AHI	9,8 (5,1-13,9)	24,9 (15,8-29,8)	45,8 (30,1-104,3)	25,5 (5,1-104,3)	88,58^{H}	<0,001*	C>B>A
Age	48 (24-63)	46,5 (27-65)	49 (30-68)	48 (24-68)	0,088^{H}	0,957	-
BMI	29,4 (18-45)	30,7 (22,9-41,9)	31,2 (22,9- 43)	30,6 (18-45)	4,956^{H}	0,084	-
MinO2sat	87 (76-94,2)	85 (72-352,5)	78,5 (47,5-88)	83 (47,5-352,5)	28,693^{H}	**<0,001***	A,B>C
TST	390,5 (44,5-486)	389,5 (224-485,5)	389,5 (141,5-565,2)	389,5 (44,5-565,2)	0,095^{H}	0,953	-
MeanO2sat	93,6 (87,6-96,7)	94 (91,1-96,1)	92,55 (79,8-95,9)	93,7 (79,8-96,7)	3,127^{H}	0,209	-
Sleep efficiency	81,9 (9,2-97,5)	82,95 (27-96,6)	80,1 (31-96,5)	81,9 (9,2-97,5)	0,213^{H}	0,899	-
Desat index	9 (1,3-18,4)	20,4 (6,6-30,9)	46,3 (15,9-319)	21 (1,3-319)	82,706^{H}	**<0,001***	C>B>A
Mean heart rate	68,5 (6,7-85,4)	70,35 (51-82,5)	70,35 (54,3-85)	70 (6,7-85,4)	1,608^{H}	0,448	-
HGB	13,59±1,43	14,56±1,68	14,62±1,54	14,27±1,6	4,721^{F}	**0,011***	B,C>A
HCT	41,40±3,96	44,11±4,46	44,34±4,33	43,31±4,42	4,981^{F}	**0,009***	B,C>A
WBC	7,47±1,55	7,70±1,62	7,61±1,69	7,59±1,61	0,163^{F}	0,850	-
PLT	259 (147-474)	238 (147-449)	245,5 (163-376)	246 (147-474)	2,829^{H}	0,243	-
MPV	10,35±0,99	10,05±1,11	10,38±1,16	10,27±1,09	0,87^{F}	0,422	-
NLR	2,01 (0,82-4,05)	1,7 (0,77-5,54)	1,49 (0,73-3,48)	1,7 (0,73-5,54)	3,202^{H}	0,202	-
MPV/PLT	0,04 (0,02-0,08)	0,04 (0,02-0,09)	0,04 (0,02-0,08)	0,04 (0,02-0,09)	1,39^{H}	0,499	-
PLR	120,4 (54,14-212,22)	103,12 (58,1-187,5)	93,49 (49,12-201,29)	103,35 (49,12-212,22)	5,151^{H}	0,076	-
IGcount	0,02 (0-0,2)	0,02 (0-0,1)	0,02 (0,01-0,9)	0,02 (0-0,9)	0,179^{H}	0,915	-
IGpercent	0,2 (0,1-0,6)	0,2 (0,1-1,1)	0,2 (0,1-1)	0,2 (0,1-1,1)	3,255^{H}	0,196	-
Plateletcrit	0,27 (0,17-0,46)	0,23 (0,18-0,39)	0,25 (0,19-0,36)	0,25 (0,17-0,46)	5,32^{H}	0,070	-
RDWCV	13,6 (12,5-18)	13,3 (11,8-14,7)	13,5 (12,6-15,5)	13,4 (11,8-18)	6,757^{H}	0,034	-
Lymphocyte	2,32 (1,07-3,75)	2,41 (0,82-5,37)	2,56 (1,49-5,7)	2,42 (0,82-5,7)	0,476^{H}	0,788	-
Neutrophil	4,35 (2,42-8,98)	4,18 (2,78-8,26)	4,335 (2,24-9,31)	4,3 (2,24-9,31)	0,199^{H}	0,905	-
WMR	0,73±0,19	0,78±0,21	0,74±0,19	0,75±0,19	0,522^{F}	0,595	-

*p<0,05 | ^{H}: Kruskal-Wallis H test ^{Z}: One-way ANOVA test

Med: median, n: Number of patients; X: Mean; SD: Standard deviation; Significant p-values are shown as bold.

Abbreviations: AHI: Apnea-Hypopnea Index; BMI: Body mass index, Min O2 sat: minimum oxygen saturation, Mean O2 sat: Mean oxygen saturation, Desat index: Desaturation index, HGB: Hemoglobin, HCT: Hematocrit,WBC: White Blood Cell; MPV: Mean Platelet Volume; RDW: Red Cell Distribution Width; NLR: Neutrophil to Lymphocyte Ratio, PLT: Platelet, PLR: Platelet to Lymphocyte Ratio, TST: Total sleep time, WMR: White Blood Cell to Mean Platelet Volume Ratio.

Table 4: Correlation between AHI scores and polysomnography, laboratory parameters in OSAS patients

		AHI
Age	rho	-0,056
	p	0,578
BMI	rho	0,259**
	p	0,009
MinO2sat	rho	-0,558**
	p	<0,001
TST	rho	-0,014
	p	0,887
MeanO2sat	rho	-,227*
	p	0,023
Sleep efficiency	rho	-0,005
	p	0,957
Desaturation index	rho	,958**
	p	<0,001
Mean heart rate	rho	0,153
	p	0,127
HGB	rho	,365**
	p	<0,001
HCT	rho	,371**
	p	<0,001
WBC	rho	0,136
	p	0,175
Platelet	rho	-0,121
	p	0,227
MPV	rho	-0,030
	p	0,769
NLR	rho	-0,135
	p	0,178
MPV/PLT	rho	0,097
	p	0,335
PLR	rho	-0,264**
	p	0,008
IGcount	rho	0,086
	p	0,401
IGpercent	rho	0,179
	p	0,080
Plateletcrit	rho	-0,117
	p	0,244
RDWCV	rho	-0,068
	p	0,500
Lymphocyte	rho	0,129
	p	0,198
Neutrophil	rho	0,060
	p	0,551
WBCMPV	rho	0,141
	p	0,159

these results might reflect a variety of factors, such as study design, exclusion criteria, sample size and genetic heterogeneity of the study population. Our study population could not be so large but had well-designed sampling criteria to investigate the utility of selected parameters.

Clinically, inflammatory markers WBC and WMR have been shown to predict prognosis, morbidity and mortality in cardiovascular diseases. Several studies have shown the diagnostic superiority of WMR values in comparison to other CBC values (e.g., WBC, MPV, PLR and NLR).[13,27,28] Zorlu *et al*. found WMR values higher in mild and moderate OSAS than in control and severe OSAS groups.[13] They claimed that WMR may be better than the other parameters in determining the severity of OSAS and may be used to distinguish severe OSAS. Also in our study, we found higher WMR values in patient groups, especially in moderate OSAS, than in control and other subgroups.

It has been assumed that intermittent hypoxia is sufficient to produce secondary polycythemia.[29] Fan *et al*. found that HGB and HCT significantly correlated with AHI and that HCT might be a predictor of OSAS severity.[24] Relevant meta-analyses provided the same results.[29,30] Several animal studies also indicated that red blood cell (RBC) count, HGB and HCT were much higher after exposure to intermittent hypoxia.[31,32] After continuous positive airway pressure (CPAP) therapy, RBC count, HGB, and HCT declined in patients with OSAS.[33] In our study, we found similar results: HGB and HCT values were high in OSAS patients and increased parallel to disease severity.

In several recent studies, IGc has been recommended as a new indicator of systemic inflammation, and its prognostic and predictive role has been shown in many diseases.[5,6] The increase of IGc is an indicator of bone marrow activation before onset of leukopoiesis, which may indicate a response to inflammatory conditions or pregnancy.[34-38] IGc an can be easily detected automatically with new-generation haemogram devices. Recent studies have demonstrated that IGc can be used as an effective inflammatory marker.[34,39-42]

Park *et al*. suggested that IGc might be an indicator of mortality due to sepsis.[39] It was shown that there is a correlation between increasing IG values and positive blood cultures.[42] İncir *et al*. reported that IGc together with haemogram parameters enabled early detection of inflammation and infection.[43] A study conducted

by Karakulak *et al*. showed that high IGc values could indicate both disease severity and mortality in patients with acute pancreatitis[44], and it was suggested that IG value had higher sensitivity and specificity in predicting inflammatory response in patients with serious bacterial infections.[38] In our study we found IGc and IG% values to be significantly higher in the OSAS group than the control group. In sub-group analysis of OSAS patients, these levels increased in parallel with the severity of OSAS but did not reach a statistically significant level.

In conclusion, to the best of our knowledge, no study in the literature has examined the relationship between OSAS and IGc**.** In this retrospective single-center study, elevated IGc, HGB, HCT, WBC, and WMR levels, along with decreased PLR values, were identified as potential biomarkers indicating increased inflammation in OSAS. This study has several limitations. Because the study was conducted in a single centre the sample size could not be so large. Changes in IGc pre-CPAP and post-CPAP treatment were not investigated. Further prospective multi-centre studies are needed to explore the association between IGc and the presence and severity of OSAS.

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