

## The Severity of Obstructive Sleep Apnea Syndrome is related to Red Cell Distribution Width and Hematocrit Values

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### Abstract

**Background:** Obstructive sleep apnea syndrome (OSAS) is a common sleep disorder characterized by recurrent upper airway collapse during sleep. Recently, some hematological parameters as red cell distribution width (RDW), mean platelet volume (MPV), and platelet distribution width (PDW) have been emerged as inflammatory biomarkers. Limited, controversial data is available on the association between these hematological parameters and the severity of OSAS. Therefore, we aimed to investigate the levels of these parameters in patients with OSAS and its correlation with the severity of OSAS.

**Methods:** The clinical data, polysomnography and laboratory results of complete blood pictures of 116 patients with OSAS were retrospectively collected and statistically analyzed.

**Results:** Obstructive sleep apnea syndrome was associated with increased levels of hematocrit, RDW, MPV, PDW, and platelets count. RDW is positively correlated with Apnea-hypopnea index, oxygen desaturation index, Epworth sleepiness scale, and negatively correlated with minimum oxygen saturation and rapid eye movement sleep.

**Conclusion:** RDW may be a marker for the severity of OSAS. As RDW is included in a complete blood count, it could provide an easy, inexpensive tool for triaging OSAS patients for polysomnography evaluation.

**Keywords:** Erythrocyte indices; Mean platelet volume; Polysomnography; Obstructive sleep apnea; Sleep disorders

### Introduction

Obstructive sleep apnea syndrome (OSAS) is a common sleep disorder characterized by recurrent upper airway collapse during sleep. This results in a reduction or complete cessation of the airflow that leads to arousals, sleep fragmentation, and oxyhemoglobin desaturation. Patients with OSAS undergo repetitive episodes of hypoxia and reoxygenation that may have systemic effects [1-3], so that, OSAS is considered a systemic inflammatory disease, not a local abnormality [4,5].

Recently, some hematological parameters have emerged as inflammatory biomarker in various diseases. Red cell distribution width (RDW), a laboratory measure of the variability of red blood cell sizes, is the index of the erythrocyte heterogeneity. RDW is calculated by division of standard deviation (SD) of RBC volume by MCV [6]. RDW is widely used to identify the potential cause of anemia. Increased values have however been recently reported in several cardiovascular disorders, such as coronary artery disease [7], heart failure [8,9], and stroke [10]. Moreover, RDW is also associated with all-cause, cardiac and non-cardiac mortality [11].

The mean platelet volume (MPV), that measure platelet size, has been considered as a marker and determinant of platelet function.

Increased MPV may reflect either increased platelet activation or increased numbers of large, hyper-aggregated platelets [12], and may represent a link between hypercoagulability and inflammation [13]. Another marker of platelet activation is the platelet distribution width (PDW) [14].

Red cell and platelets indices have been extensively investigated in various diseases. Limited, controversial information is available, however, on the association between red cell [15-19] and platelets [15, 20-25] parameters and the severity of OSAS. Therefore, the aim of this study was to investigate the levels of these parameters in patients with OSAS and to assess whether there is any correlation between the severity of OSAS and any of these parameters.

### Material and Methods

Between January 2011 and June 2014 a total of 264 patients admitted to the sleep unit underwent a polysomnographic evaluation and were diagnosed as OSAS patients. 116 out of the 264 met the inclusion and exclusion criteria of this study and were enrolled in this study. Inclusion criteria were patients who are with symptoms of nocturnal snoring and/or excessive daytime sleepiness. Exclusion criteria were any known cardiac disease (congestive heart failure, ischemic vascular disease, or arrhythmias), lung disease (chronic obstructive pulmonary disease, asthma and IPF), diabetes mellitus, hypertension, smoking, and chronic renal or hepatic diseases, a history of recent blood transfusion (three weeks), and known hematologic

disease such as leukemia or myelodysplastic syndrome. Patients diagnosed with obesity hypoventilation, overlap syndrome, complex sleep apnea, central sleep apnea, Cheyne-Stokes sleeping disorder, or REM-induced OSAS were excluded from the PSG results. These patients were excluded because these diseases have comorbidities that could cause inflammation.

Detailed medical history, physical examination, routine laboratory investigations, a respiratory function test, electrocardiogram (ECG), and chest X-ray were assessed. Initially, patients were already grouped into three OSAS severity categories: mild (AHI 5 to <15), moderate (AHI 15 to <30), and severe (AHI >30). Further, we combined mild and moderate groups into one group (AHI 5 to <30). As a control group, 62 individuals (ages 44-63) diagnosed with simple snoring (AHI <5) were chosen.

**Polysomnographic sleep study:** In sleep-laboratory, all patients had been assessed regarding their degree of OSAS by subjecting them to basic full night formal PSG sleep study (sleep screen recorder viasys company Germany) in the supine position for definitive diagnosis. PSG was performed and scored according to standard criteria using nasal pressure cannula and tracheal sounds (suprasternal microphone) for airflow measurement. Respiratory events were scored manually. Apnea was defined as cessation of airflow for  $\geq 10$  s. Hypopnea was defined as a 30% reduction accompanied by a 4% decrease in capillary oxygen saturation (SpO<sub>2</sub>) of airflow or a 50% reduction of airflow accompanied by a 3% decrease in SpO<sub>2</sub>. Classification of a hypopnea as obstructive, central, or mixed performed calibrated respiratory inductance plethysmography. Hypopnea was classified as obstructive in the presence of continued movement in the respiratory inductive plethysmograph (RIP). The oxygen desaturation index (ODI) is the number of times per hour of sleep in which the blood's oxygen level drops by 3 percent or more from baseline. The apnea hypopnea index was taken as the average number of apnea and hypopnea events per hour of sleep. Epworth Sleepiness Scale (ESS) consists of eight questions answered by the patient with regard to daily activities measured on a scale of zero to three and having proportionate values starting from a minimum of zero to a maximum of twenty-four points.

Measurement of laboratory parameters. Fasting (8 hours) venous blood samples were drawn from the antecubital vein, using a sterile

21-gage needle syringe without stasis, between 8 and 9 AM after polysomnography and after 20 min rest. Tripotassium ethylenediaminetetraacetic acid (K<sub>3</sub> EDTA) based anticoagulated blood samples were drawn in Vacutainer tubes (Vacutainer, Becton, Dickinson and Company, Franklin Lakes, NJ, USA) and standardized to be assessed within 30 minutes from blood sampling time. Complete blood counts were performed using the Abbott Cell-Dyne 3700 System (Abbott Diagnostics, Santa Clara, CA, USA).

**Statistical Analysis.** All variables were tested for normality with the Kolmogorov-Smirnov test. Normally distributed continuous variables are expressed as mean  $\pm$  standard deviation. Non-normally distributed continuous variables are summarized as medians. Categorical variables are expressed as numbers (percentages). Comparisons between independent groups were made using the Mann-Whitney test. Correlations between non-continuous variables and continuous variables with a non-normal distribution were assessed using Spearman's correlation. Correlations between continuous variables were assessed using Pearson's correlation. Univariate and multivariate linear regression analysis were performed to determine the independent correlations of studied parameters. value<0.05 was considered statistically significant. The statistical analysis was performed with SPSS for Windows version 18.0 (SPSS, Chicago, IL, USA).

## Results

### Patient characteristics

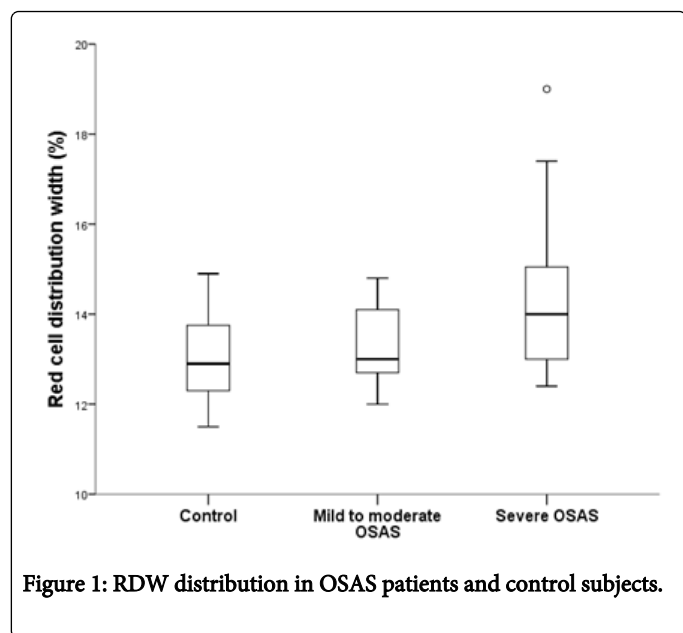
The demographic and clinical characteristics of the patients and controls are shown in Table 1. The patients in this study were subdivided according to AHI into mild, moderate, combined mild and moderate and severe OSAS. We included a total of 116 patients with OSAS [34 patients (29.3%) mild, 20 patients (17.3%) moderate and 62 patients (53.4%) severe] and 62 simple snoring control cases. There were no statistically significant differences between the two groups regarding Age, sex distribution, and BMI. There was no lung disease in both groups.

|                                       | Control<br>(n=62) | Total patients<br>(n=116) | Mild to moderate<br>(n=54) | Severe<br>(n=62) | P1      | P2      | P3      | P4      | P5      |
|---------------------------------------|-------------------|---------------------------|----------------------------|------------------|---------|---------|---------|---------|---------|
| <b>AHI (events/hour)</b>              | 0.9 (0.2-3.2)     | 34.5 (5.2-105)            | 12 (5.2-27.7)              | 58 (30-105)      |         |         |         |         |         |
| <b>Age (years)</b>                    | 51 (44-63)        | 51 (39-70)                | 50 (40-65)                 | 51 (39-70)       | 0.99    | 0.523   | 0.667   | 0.465   | 0.521   |
| <b>BMI (kg/m<sup>2</sup>)</b>         | 32.3 (25.5-36.6)  | 32.8 (23-43.4)            | 32.5 (23-40)               | 34.8 (28-43.4)   | 0.184   | <0.001* | 0.036*  | 0.142   | <0.001* |
| <b>Polysomnographic study results</b> |                   |                           |                            |                  |         |         |         |         |         |
| Oxygen Desaturation Index             | 1.2 (0.4-3.5)     | 38 (0.9-105)              | 12 (0.9-38)                | 62 (31-105)      | <0.001* | <0.001* | <0.001* | <0.001* | <0.001* |
| Minimum Oxygen Saturation             | 92 (91-94)        | 76.5 (42-93)              | 84 (54-93)                 | 68 (42-88)       | <0.001* | <0.001* | <0.001* | <0.001* | <0.001* |
| Basal Oxygen Saturation               | 97.3 (96.3-98.5)  | 93 (79-98)                | 93 (80-98)                 | 92 (79-95.5)     | <0.001* | <0.001* | 0.011*  | <0.001* | 0.084   |
| Epworth Sleepiness Scale              | 5 (2-8)           | 11 (4-17)                 | 7 (4-13)                   | 13 (4-17)        | <0.001* | <0.001* | <0.001* | <0.001* | <0.001* |

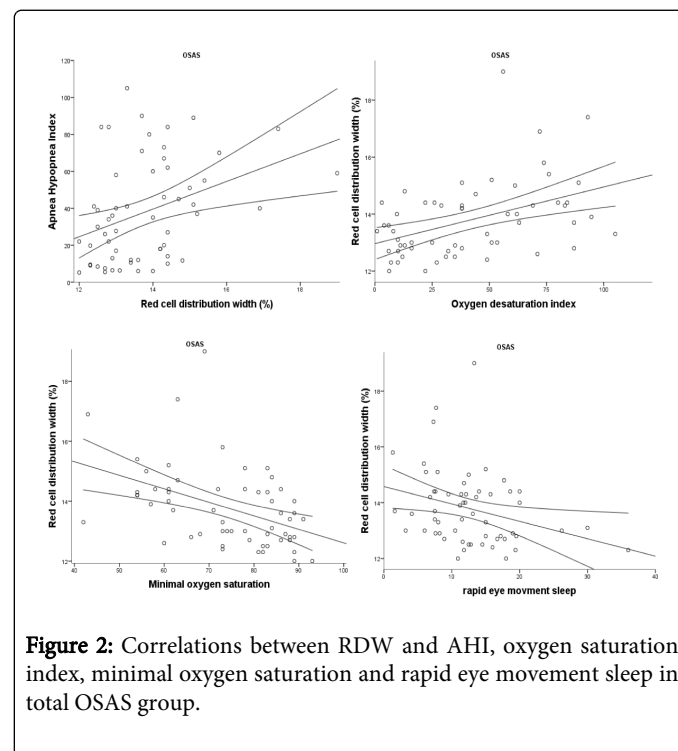
|                             |                  |                 |                  |                  |         |         |        |         |        |
|-----------------------------|------------------|-----------------|------------------|------------------|---------|---------|--------|---------|--------|
| Sleep Efficiency            | 92.9 (88-96.5)   | 85.7 (37.8-99)  | 85.9 (37.8-94)   | 85 (64-99)       | <0.001* | 0.001*  | 0.488  | <0.001* | 0.44   |
| Rapid Eye Movement sleep    | 23.1 (20.6-25)   | 11.9 (1.3-36)   | 13.6 (4.1-36)    | 11.6 (1.3-20)    | <0.001* | <0.001* | 0.010* | <0.001* | 0.040* |
| <b>Laboratory variables</b> |                  |                 |                  |                  |         |         |        |         |        |
| WBC (X109/L)                | 6.2 (4-9.8)      | 7.1 (3.9-11)    | 6.2 (3.9-9.8)    | 7.4 (4.1-11)     | 0.183   | 0.087   | 0.152  | 0.606   | 0.289  |
| RBCs (X106/L)               | 5.11 (4.5-6.1)   | 5.14 (3.4-7.1)  | 5.16 (3.4-7.1)   | 5.13 (4-5.9)     | 0.213   | 0.436   | 0.521  | 0.129   | 0.356  |
| Hemoglobin (g/dL)           | 13.2 (10.8-15.2) | 13.5 (9.9-16.9) | 13.8 (9.9-16)    | 13.5 (10.8-16.9) | 0.29    | 0.394   | 0.407  | 0.422   | 0.956  |
| Hematocrit (%)              | 45.4 (40-50.1)   | 45 (39.9-54.3)  | 43.4 (39.9-49.5) | 45.1 (40.1-54.3) | 0.701   | 0.916   | 0.215  | 0.193   | 0.143  |
| MCV                         | 86 (80.1-94.9)   | 85 (65.3-95.3)  | 85 (77.9-95.3)   | 85.4 (65.3-94.3) | 0.068   | 0.113   | 0.468  | 0.198   | 0.714  |
| RDW (%)                     | 12.9 (11.5-14.9) | 13.6 (12-19)    | 13 (12-14.8)     | 14 (12.4-19)     | 0.010*  | 0.001*  | 0.028* | 0.408   | 0.008* |
| Platelet count (X109/L)     | 222 (158-347)    | 193 (91-384)    | 198 (121-384)    | 189 (91-361)     | 0.040*  | 0.086   | 0.588  | 0.07    | 0.845  |
| MPV (fl)                    | 8.6 (7.5-9.6)    | 10.9 (8.2-14.6) | 10.9 (8.3-13.8)  | 11 (8.2-14.6)    | <0.001* | <0.001* | 0.308  | <0.001* | 0.634  |
| PDW (fl)                    | 13.4 (9.4-15.1)  | 14.7 (9.4-21.9) | 13.9 (9.8-21.9)  | 14.9 (9.4-20)    | 0.014*  | 0.005*  | 0.113  | 0.177   | 0.888  |

**Table 1:** Demographic, clinical and laboratory characteristics of studied groups. (P1: Comparison between total patients versus control group. P2: Comparison between severe versus control group. P3: Comparison between mild, moderate and severe. P4: Comparison between mild+ moderate versus control. P5: Comparison between severe versus mild+ moderate. Categorical variables are expressed in frequency (percentage); numerical variables are expressed in median (range). AHI: Apnea-hypopnea index; BMI: body mass index; WBC: White blood cells; RBCs: Red blood cells; RDW: Red cell distribution width; PDW: Platelets distribution width; MPV: Mean platelet volume, \*Significant).

OSAS patients had significantly higher oxygen desaturation index, Epworth sleepiness scale and significantly lower minimal, basal oxygen saturation, sleep efficiency and rapid eye movement sleep when compared to control subjects. In addition, RDW was significantly higher in OSAS, severe OSAS versus control subjects and severe versus mild to moderate OSAS (Table 1 and Figure 1). Moreover, platelets count was significantly higher in OSAS. In addition, MPV was significantly higher in OSAS, mild to moderate and severe OSAS versus control subjects.



Moreover, PDW was significantly higher in OSAS and severe OSAS versus control subjects (Table 1). Furthermore, there was a significant negative correlation between hematocrit and minimal oxygen saturation in mild to moderate OSAS group ( $r=-0.479$ ,  $p=0.011$ , data not shown).



In the patient population, AHI showed significantly positive correlation with oxygen desaturation index, Epworth sleepiness scale, hematocrit, RDW and significantly negative correlation with minimal oxygen saturation, and basal oxygen saturation in OSAS group (Table

2). Moreover, RDW showed significantly positive correlation with oxygen desaturation index, Epworth sleepiness scale, hematocrit and significantly negative correlation with minimal oxygen saturation and rapid eye movement sleep in OSAS group (Table 2 and Figure 2).

|                           | AHI    |         | RDW    |         | Hematocrit |        | MPV    |         | PDW    |         |
|---------------------------|--------|---------|--------|---------|------------|--------|--------|---------|--------|---------|
|                           | r      | p       | r      | p       | r          | p      | r      | p       | r      | p       |
| Oxygen Desaturation index | 0.917  | <0.001* | 0.437  | 0.001*  | 0.047      | 0.020* | 0.047  | 0.726   | 0.042  | 0.757   |
| Minimum oxygen saturation | -0.644 | <0.001* | -0.456 | <0.001* | -0.035     | 0.052  | -0.035 | 0.793   | -0.064 | 0.631   |
| Basal oxygen saturation   | -0.363 | 0.005*  | -0.204 | 0.125   | 0.089      | 0.063  | 0.089  | 0.506   | -0.129 | 0.335   |
| Epworth sleepiness scale  | 0.816  | <0.001* | 0.365  | 0.005*  | -0.001     | 0.051  | -0.001 | 0.993   | -0.012 | 0.929   |
| Sleep efficiency          | 0.098  | 0.463   | -0.084 | 0.53    | 0.129      | 0.749  | 0.129  | 0.334   | 0.223  | 0.092   |
| Rapid eye movement sleep  | -0.183 | 0.169   | -0.321 | 0.014*  | 0.018      | 0.004* | 0.018  | 0.892   | 0.107  | 0.423   |
| WBC (X109/L)              | 0.108  | 0.42    | 0.246  | 0.062   | 0.204      | 0.016* | 0.204  | 0.125   | -0.114 | 0.392   |
| RBCs (X106/L)             | -0.008 | 0.955   | 0.222  | 0.094   | 0.375      | 0.444  | 0.375  | 0.004*  | 0.319  | 0.015*  |
| Hemoglobin (g/dL)         | 0.002  | 0.991   | -0.023 | 0.864   | 0.214      | 0.057  | 0.214  | 0.106   | 0.207  | 0.119   |
| Hematocrit (%)            | 0.26   | 0.049*  | 0.618  | <0.001* | -          | -      | 0.162  | 0.225   | 0.766  | 0.074   |
| RDW (%)                   | 0.399  | 0.002*  | -      | -       | 0.618      | 0.162  | 0.214  | 0.107   | 0.141  | 0.766   |
| Platelets count (X109/L)  | 0.081  | 0.544   | -0.08  | 0.552   | -0.36      | 0.326  | -0.36  | 0.006*  | -0.511 | <0.001* |
| PDW (fl)                  | 0.065  | 0.629   | 0.141  | 0.292   | 0.766      | 0.074  | 0.766  | <0.001* | -      | -       |
| MPV (fl)                  | 0.099  | 0.458   | 0.214  | 0.107   | 0.162      | 0.225  | -      | -       | 0.766  | <0.001* |

**Table 2:** Correlations between different parameters in OSAS patients group (AHI: Apnea-Hypopnea Index; WBC: White Blood Cells; RBCs: Red Blood Cells; RDW: Red Cell Distribution Width; PDW: Platelets Distribution Width; MPV: Mean Platelet Volume, \*Significant).

Hematocrit showed significantly positive correlation with oxygen desaturation index, WBCs, MCV and significantly negative correlation with rapid eye movement sleep in OSAS group. Additionally, Hematocrit showed significantly positive correlation with PDW and significantly negative correlation with minimal oxygen saturation in mild to moderate OSAS group (Table 2).

### Linear regression analysis

Independent variables including age, body mass index, apnea-hypopnea index, and oxygen desaturation index were applied as

covariates in linear analysis. The multivariate analysis including variables which showed  $p < 0.05$  at univariate analysis (AHI and oxygen desaturation index) was done. Only oxygen desaturation index is an independent predictor of RDW, and higher oxygen desaturation index is a predictor of higher RDW ( $\beta = 0.035$ ,  $p = 0.023$ ) ( $p = 0.016$ ,  $OR = 1.088$ ,  $95\% \text{ CI} = 1.016 - 1.165$ ) (Tables 3 and 4). Multiple regression analysis was done on all other outcomes, namely hematocrit, MPV, and PDW. However all results were non-significant (data are not shown).

|                      | $\beta$ coefficient | SE    | p     |
|----------------------|---------------------|-------|-------|
| Age (years)          | 0.014               | 0.020 | 0.470 |
| Body mass index      | 0.011               | 0.019 | 0.568 |
| Apnea-hypopnea index | -0.019              | 0.016 | 0.246 |

|                           |       |       |       |
|---------------------------|-------|-------|-------|
| Oxygen Desaturation Index | 0.035 | 0.015 | 0.023 |
|---------------------------|-------|-------|-------|

**Table 3:** Predictors of red cell distribution width by linear regression analysis.

|                           | Univariate |       |          | Multivariate |        |       |          |
|---------------------------|------------|-------|----------|--------------|--------|-------|----------|
|                           | p          | OR    | 95% C.I. |              | p      | OR    | 95% C.I. |
| Age                       | 0.287      | 1.041 | 0.967    | 1.121        |        |       |          |
| Body Mass Index           | 0.759      | 1.011 | 0.943    | 1.085        |        |       |          |
| Apnea-Hypopnea Index      | 0.007*     | 1.031 | 1.009    | 1.054        | 0.141  | 0.95  | 0.888    |
| Oxygen Desaturation Index | 0.001*     | 1.038 | 1.015    | 1.062        | 0.016* | 1.088 | 1.016    |
| Hemoglobin.               | 0.968      | 1.008 | 0.696    | 1.46         |        |       |          |

**Table 4:** Independent predictors of red cell distribution width by multivariate logistic regression analysis (\*Significant).

## Discussion

This study is a comprehensive one of only a few controversial studies examining the relationship between almost-single-hematological parameter and AHI in OSAS. We have shown that RDW, MPV, and PDW are higher in OSAS. Additionally, hematocrit and RDW are positively correlated with AHI. These findings reveal the importance of full blood count and indices in OSAS patients, and suggest that hematocrit and RDW might be a related marker of OSAS severity.

Recently, the concept of OSAS as a simple respiratory abnormality during sleep has been diverted to a systemic response due to multiple pathogenetic mechanisms of oxidative stress [26-30], increased sympathetic **overactivity** [31], coagulation fibrinolysis imbalance, and platelets activation [32]. All these factors lead to a state of systemic inflammation [4, 33-35], endothelial dysfunction [3], metabolic dysregulation [36], and hypercoagulability [32].

Red cell distribution width indicates the variability in the size of blood erythrocytes. RDW is measured by automated hematology analyzers as part of a complete blood count [37]. The exact mechanism of a high RDW level in patients with OSAS and its association with AHI is not clear. However, this may be related to oxidative stress and chronic inflammation in OSAS, both playing major roles in the pathogenesis of OSAS. Oxidative stress has been shown to be associated with RDW and antioxidants were shown to be significantly associated with a decrease in RDW [38]. Additionally, A state of chronic inflammation exists in OSAS and lead to increased secretion of interleukin-6 (IL-6) and other pro-inflammatory cytokines [39,40]. RDW may reflect the bone marrow's response to systemic, ongoing inflammation [41]. Inflammation may influence erythropoiesis, erythrocyte circulatory half-life and erythrocyte deformability, promoting anisocytosis and thus increasing RDW levels [40]. Recently, it was demonstrated that greater RDW levels were independently associated with greater high-sensitivity CRP levels, a well-established marker of inflammation [39,41]. Further, high RDW levels may be related to increased neurohormonal activity in OSAS [42].

Our results may appear similar to previous two studies in literature [16,17], regarding the elevation and correlation of RDW to the severity of AHI. However, there is a major difference in the study design between these two studies and ours. We have designed the current

study cautiously, to avoid confounding diseases; that may affect RDW results, so that no difference between patients and controls regarding comorbidity diseases. In contrast, these previous studies [16,17], that have not excluded or equalize the effect of comorbidity as coronary artery disease [7,11], diabetes mellitus [43], and hypertension [44], which could lead to elevation of RDW.

In addition to its positive correlation with the severity of OSAS, RDW was also associated with most of the sleep parameters in patients with OSAS. More specifically, RDW was positively correlated with oxygen desaturation index, Epworth sleepiness scale (EES), an established marker of daily sleepiness [45], and negatively correlated with both of minimum oxygen saturation rapid eye movement (REM) sleep. This supports our proposed role of RDW as a simple surrogate marker for the severity of OSAS. To the best of our knowledge, these all associations have not been reported before.

Blood viscosity is defined as the internal resistance of the blood to shear forces. Blood viscosity is determined by plasma viscosity, hematocrit (volume fraction of erythrocytes, which constitute 99.9 % of the cellular elements), and the mechanical behavior of erythrocytes [46]. Thus, hematocrit plays an important role in blood coagulability, as it affects blood viscosity and platelet aggregation, and hypoxic individuals often have increased hematocrit [47]. Increased blood clotting, caused by changes in the rheological properties (flow properties) of blood and plasma, seems to be an important factor linking OSAS and CV complications [48]. In this study, although hematocrit levels were not increased in patients with OSAS, hematocrit was positively correlated with AHI, the severity of index of OSAS. In literature, few studies have determined that patients with OSAS have increased hematocrit levels [49-54], and only one study revealed that the hematocrit correlate positively with OSAS severity [49], similar to this study. However, Reinhart et al. [54] found no relation between hematocrit and the severity of OSAS. Both short-term, and long-term CPAP therapy were found to decrease hematocrit levels in OSAS patients [52,55].

Patients with OSAS have a complex array of factors that may result in a state of hypercoagulability [32]. Hypoxemia experienced by patients during apnea triggers the release of inflammatory factors that alter the micromilieu of the blood, resulting in hypercoagulability [56]. Regarding platelets, the major finding of this study was that, compared

to the control, MPV and PDW were increased in total group subjects with OSAS, and in patients with severe OSAS. Additionally, platelets count was increased in total group subjects with OSAS. This may support the evidence for platelet activation in OSAS, which may contribute to the increased incidence of cardiovascular events in patients with OSAS [57,58]. Moreover, this study is the first to demonstrate elevated platelets count in patients with OSAS. However, no correlations were found between any of these platelets indices and severity of OSAS or the sleep parameters, contrary to our results of RDW, and hematocrit. In this study, we excluded the possible confounding effects of several factors/diseases on the studied hematological parameters, as hypertension, cardiovascular diseases, smoking, and diabetes mellitus. There were no statistical differences regarding these factors between OSAS patients and controls.

There is controversy about MPV and PDW levels in patients with OSAS. Varol et al. [19] found that MPV was significantly higher in patients with severe OSAS when compared with control subjects and MPV was correlated with AHI. Alternatively, the results of the study of Kurt et al. [15] revealed that PDW, but not MPV, was higher in severe OSAS. In accordance with our results, Nena et al. [20] reported that both of MPV and PDW levels were significantly higher in severe OSAS patients than in control and mild to moderate OSAS. However, their study did not exclude cardiac or lung disease, chronic renal or hepatic disease, hypertension, or smoking.

The exact mechanism of platelet activation in patients with OSAS is unclear and may be complex, Three main pathways may be implicated; sympathetic overactivity [59], hypoxia [60], and inflammation [61,62], all being well-known features of OSAS [3-5].

There are potential limitations of this study. First, as it is a retrospective study, we did not include a marker of inflammation, neurohormonal activation, or oxidative stress to evaluate its correlation with these CBC parameters. Second, this study cannot discriminate causality from association with regard to the link between RDW and OSAS in relation to inflammation and oxidative stress. Third, this is not a follow-up study, so we do not have the prognostic outcome results of OSAS patients with high RDW values, including the influence of CPAP therapy on these patients. Fourth, we did not measure nutritional status of vitamin B and folate levels, which are one of the potential causes of increased levels of RDW. However, our study population is not anemic, and the possible effect of these vitamins deficiencies can be neglected.

## Conclusions

In conclusion, our study has established that RDW, MPV, PDW, and platelets count all are increased in OSAS. RDW is positively correlated with AHI, oxygen desaturation index, EES, and negatively correlated with minimum oxygen saturation and REM sleep. Thus, RDW may be a marker for the severity of OSAS. As RDW is included in a complete blood count, it could provide an easy, inexpensive tool for triaging OSAS patients for polysomnography evaluation. It is highly possible that RDW will become one of the items of the standard evaluation test panel for OSAS patients and patients with severe OSAS could be identified based on RDW at the first examination and given priority for testing and treatment.

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