

# Differences and Risk Factors of Peripheral Blood Immune Cells in Patients with Obstructive Sleep Apnea

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**Introduction:** Obstructive sleep apnea (OSA) is a respiratory disorder characterized by chronic intermittent hypoxia and fragmented sleep, leading to inflammatory response and oxidative stress. However, the differences in immune inflammatory response in OSA patients with different severity remain unclear.

**Purpose:** This study aims to examine the differences in peripheral blood immune cells and their risk factors in OSA patients.

**Patients and Methods:** A total of 277 snoring patients from the Sleep Respiratory Disorder Monitoring Center of Zhongnan Hospital of Wuhan University were recruited in this study. According to the diagnosis and severity criteria of OSA, the included patients were further divided into simple snoring, mild, moderate, and severe groups. Peripheral blood immune cell counts including white blood cells, neutrophils, lymphocytes, monocytes, eosinophils, basophils, red blood cells, platelets, and polysomnography indicators were collected from the patients.

**Results:** Compared with simple snoring patients, the OSA patients had increased circular monocyte and basophil count levels. In addition, correlation analysis results indicated that monocyte count was positively associated with chronic obstructive pulmonary disease (COPD), smoking, apnea-hypopnea index (AHI), the longest apnea duration, and Oxygen desaturation index (ODI), and negatively correlated with average SpO<sub>2</sub> in snoring patients. Finally, multiple linear regression analysis revealed that AHI, COPD, smoking, and maximum heart rate were independent predictors of monocyte count.

**Conclusion:** OSA patients had a significant increase in their peripheral blood monocyte count. AHI, COPD, smoking, and maximum heart rate were risk factors for increased peripheral blood monocyte count in OSA patients. These findings suggest that peripheral blood monocytes can be considered an inflammatory biomarker of OSA.

**Keywords:** obstructive sleep apnea, peripheral blood cell count, monocytes, polysomnography, inflammatory biomarker

## Introduction

Obstructive sleep apnea (OSA) is characterized by upper respiratory collapse, intermittent hypoxia, recurrent arousals, and sleep fragmentation. This results in secondary sympathetic nerve activation, oxidative stress, and systemic inflammation.<sup>1</sup> Inflammatory response and oxidative stress in OSA patients are risk factors for the occurrence and development of various diseases, including cardiovascular and cerebrovascular diseases, metabolic diseases, cognitive impairment, and tumors.<sup>2,3</sup> It is reported that recurrent intermittent hypoxia and increased oxidative stress during sleep play an important role in immune dysfunction in OSA patients.<sup>4-6</sup>

Previous studies found that peripheral blood cells can reflect the immune inflammatory response.<sup>7,8</sup> They often were regarded as easily measurable biomarkers of inflammation and oxidative stress in OSA, such as neutrophils, lymphocytes, monocytes, hemoglobin, and hematocrit, as well as new biomarkers including neutrophil to lymphocyte ratio

(NLR), platelet to lymphocyte ratio (PLR), and systemic inflammatory index (SII).<sup>9–11</sup> In addition, immune cell-driven inflammation also plays a crucial role in the pathogenesis of OSA. Some pro-inflammatory markers released by peripheral blood cells such as C-reactive protein (CRP), interleukin (IL)-6, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), erythrocyte sedimentation rate (ESR) were also strongly associated with OSA severity.<sup>12,13</sup> It is reported that long-term exposure to intermittent hypoxia promotes neutrophil and monocyte infiltration into the liver, leading to strong inflammatory pathways including IL-16 and TNF- $\alpha$ .<sup>14</sup> Polymorphonuclear neutrophils (PMN) are also key cells in the inflammatory process. The increased number of PMN has been found to play a potential role in the inflammation associated with OSA patients. IL-6,  $\beta_2$ -adrenergic receptor (ADRB2), and IL-8 may contribute to regulating the activation of PMN, including migration, recruitment, degranulation, exocytosis, and respiratory burst.<sup>15</sup>

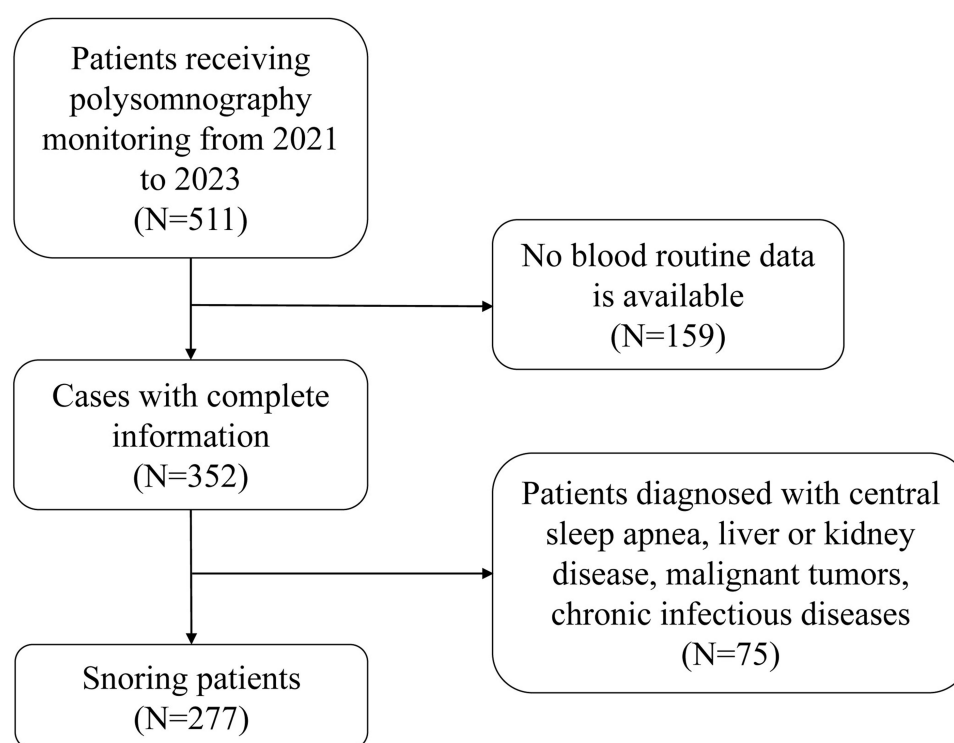
Therefore, it is crucial to explore the differences in peripheral blood immune cells in patients with obstructive sleep apnea. We assume that peripheral blood cell parameters could indicate the inflammation degree and be a predictive tool for evaluating hypoxia severity in OSA. However, the results from previous studies have been inconsistent, and the reasons for the differences in peripheral blood cells remain unclear. As a cross-sectional study, this study aimed to analyze differences in immune cells in OSA patients of different severity and identify associated risk factors.

## Materials and Methods

### Study Population

This retrospective study was approved by the Ethics Committee of Zhongnan Hospital of Wuhan University (No.2023297K, December 27, 2023) and waived written informed consent from all patients. This study collected 277 snoring patients receiving polysomnography (PSG) monitoring at the Sleep Respiratory Disorder Monitoring Center of Zhongnan Hospital of Wuhan University from 2021 to 2023. The screening process for 277 patients is shown in Figure 1.

Diagnosis and disease severity criteria for OSA were defined according to the guidelines.<sup>16</sup> The Apnea hypopnea index (AHI) was calculated as the average number of apnea and hypopnea events per hour. Snoring patients were divided into the simple snoring group (AHI <5) and the OSA group (AHI  $\geq$ 5). The severity of OSA patients was further classified into subgroups of mild ( $5 \leq$  AHI <15), moderate ( $15 \leq$  AHI <30), and severe (AHI  $\geq$ 30).<sup>17</sup> Patients diagnosed with central



**Figure 1** The screening process of 277 patients.

sleep apnea, liver or kidney disease, malignant tumors, chronic infectious diseases, inflammatory bowel disease, and hematological disorders such as leukemia, anemia, or myelodysplastic syndrome were excluded from this study.

## Data Collection

Data on the patient characteristics collected in this study included age, sex, body mass index (BMI), smoking status, and comorbidities. Peripheral blood immune cell was evaluated by complete blood count (CBC), including white blood cell (WBC), monocytes, lymphocytes, neutrophils, platelets, eosinophils, and basophils, hemoglobin, red blood cell count (RBC), NLR, PLR, systemic inflammation index (SII: neutrophils  $\times$  platelets/lymphocytes) were recorded. Additionally, AHI, Oxygen desaturation index (ODI, number of oxygen desaturations per hour of sleep), the sum of all desaturations, the longest apnea duration, the minimum and average pulse oxygen saturation ( $\text{SpO}_2$ ), the minimum, average, and maximum heart rate during PSG were collected. Apnea was defined as a more than 90% decrease in airflow for 10 seconds. Hypopneas was defined as a reduction in airflow of at least 30% lasting for 10 seconds or more, accompanied by oxygen desaturation of 3% or more, or an electroencephalogram (EEG) awakening.<sup>18</sup>

## Statistical Analysis

Continuous variables were presented as median with interquartile range (IQR). Student's *t*-test was performed for normally distributed variables, and the Mann–Whitney test was employed for non-normally distributed variables between two groups. The one-way analysis of variance (ANOVA) test was used to compare normally distributed variables, and the Kruskal–Wallis *H*-test was used for non-normally distributed variables between OSA subgroups. Categorical variables were expressed as numbers (percentages). The chi-square or Fisher's exact test was conducted for two groups, and the Kruskal–Wallis *H*-test was used for multiple groups. The Bonferroni test was conducted as a post-test for multiple comparisons. The correlation between variables was examined using Spearman's or Pearson's test. The point-biserial correlation, a special form of Pearson's test was used to assess correlation between continuous variables and dichotomous chronic disease variables. Multiple linear regression analysis was conducted to assess the independent associations between biochemical, clinical, and polysomnography variables. Data analysis used SPSS software (version 25.0, IBM Corporation). Statistical significance was set at  $P < 0.05$ .

## Results

### Demographic and Clinical Profiles

After the screening, 277 snoring patients (196 with OSA and 81 simple snoring) were included in this study. The median age of OSA patients was 45 (34–61) years, with a body mass index (BMI) of 29 (25.4–33.2)  $\text{kg/m}^2$  and 117 (59.7%) being male. The proportion of smokers, hypertension, diabetes, chronic obstructive pulmonary disease (COPD), and asthma in OSA patients was 21.3%, 39.8%, 15.8%, 8.2%, and 7.7%, respectively. There were significant differences in BMI ( $P = 0.009$ ), age ( $P < 0.001$ ), sex ( $P < 0.001$ ), hypertension ( $P < 0.001$ ), and smoking ( $P = 0.004$ ) between the simple snoring and OSA group. Furthermore, significant differences were shown in age ( $P < 0.001$ ), hypertension ( $P < 0.001$ ), and smoking ( $P = 0.017$ ) between subgroups. The detailed demographic and clinical data are shown in Table 1.

### Differences in Blood Immune Cells in Snoring Patients

The hematological profiles are shown in Table 2. Compared with the simple snoring group, the OSA patients had increased levels of peripheral blood monocyte ( $P < 0.001$ ) and basophil ( $P = 0.012$ ) counts. After conducting a post hoc analysis, there was a significant difference in the monocyte count between the simple snoring group and the severe OSA group ( $P = 0.001$ ). Additionally, the post-test results showed a statistically significant difference in basophil count between the simple snoring group and the moderate OSA group ( $P = 0.036$ ). No significant differences were observed in other peripheral blood parameters (Table 2).

**Table 1** Clinical Characteristics of Snoring Patients

	Total (N=277)	Simple Snoring (N=81)	OSA (N= 196)	Mild (N= 80)	Moderate (N=46)	Severe (N=70)	P <sup>a</sup>	P <sup>b</sup>
<b>Sex</b>							<b>&lt;0.001</b>	<b>&lt;0.001<sup>b,c,d</sup></b>
Male	141 (50.9)	24 (29.6)	117 (59.7)	41 (51.2)	27 (58.7)	49 (70)		
Female	136 (49.1)	57 (70.4)	79 (40.3)	39 (48.8)	19 (41.3)	21 (30)		
<b>Age (years)</b>	44 (32–59)	35 (28.5–47)	45 (34–61)	45 (31–60)	54 (39.25–66.25)	51.5 (38.75–61.75)	<b>&lt;0.001</b>	<b>&lt;0.001<sup>b,c,d</sup></b>
<b>BMI (kg/m<sup>2</sup>)</b>	30 (26–33.9)	32.8 (27–34.6)	29 (25.4–33.2)	29.1 (25–34.3)	29 (26–33.08)	28.2 (26.0–32.13)	<b>0.009</b>	0.063
<b>Comorbidities</b>								
Hypertension	87 (31.4)	9 (11.1)	78 (39.8)	23 (28.7)	22 (47.8)	33 (47.1)	<b>&lt;0.001</b>	<b>&lt;0.001<sup>b,c</sup></b>
Coronary disease	16 (5.8)	5 (6.2)	11 (5.6)	3 (3.8)	4 (8.7)	4 (5.7)	1	0.702
Diabetes	44 (15.9)	13 (16)	31 (15.8)	15 (18.8)	10 (21.7)	6 (8.6)	0.962	0.215
COPD	20 (7.2)	4 (4.9)	16 (8.2)	8 (10)	4 (8.7)	4 (5.7)	0.346	0.597
Asthma	16 (5.8)	1 (1.2)	15 (7.7)	9 (11.3)	3 (6.5)	3 (4.3)	0.072	0.045
<b>Smoking</b>	49 (17.7)	6 (7.4)	43 (21.3)	17 (28.3)	13 (26.92)	13 (21.21)	<b>0.004</b>	<b>0.017<sup>c</sup></b>

**Notes:** Data are presented as median (IQR) or n (%). P<sup>a</sup> indicates differences between simple snoring and OSA groups. \*The Kruskal–Wallis H-test or Chi-square test (post hoc: Bonferroni). <sup>b</sup>Comparison between simple snoring and severe OSA group. <sup>c</sup>Comparison between simple snoring and moderate OSA. <sup>d</sup>Comparison between simple snoring and mild OSA. Bold values indicate statistical differences. The criteria for hypertension: without the use of antihypertensive drugs, the systolic blood pressure (SBP) in the examination room is  $\geq 140$  mmHg and/or the diastolic blood pressure (DBP) is  $\geq 90$  mmHg. The criteria for coronary disease: coronary atherosclerotic heart disease, refers to the heart disease caused by myocardial ischemia, hypoxia or necrosis due to stenosis or occlusion of the lumen caused by coronary atherosclerosis. The criteria for diabetes: fasting plasma glucose  $\geq 7.0$  mmol/L or 2-h plasma glucose  $\geq 11.1$  mmol/L during oral glucose tolerance test or glycohemoglobin A1C  $\geq 6.5\%$  or in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose  $\geq 11.1$  mmol/L.

**Abbreviations:** BMI, body mass index; COPD, chronic obstructive pulmonary disease.

## Polysomnographic Parameters in Snoring Patients

The polysomnography indicators in snoring patients are presented in Table 3. There were significant differences in AHI ( $P < 0.001$ ), the longest apnea duration ( $P < 0.001$ ), the sum of all desaturations ( $P < 0.001$ ), ODI ( $P < 0.001$ ), minimum SpO<sub>2</sub> ( $P < 0.001$ ), average SpO<sub>2</sub> ( $P < 0.001$ ), and minimum heart rate ( $P < 0.001$ ) between OSA patients and simple snoring patients. Moreover, significant differences were observed in AHI, the longest apnea duration, the sum of all desaturations, and ODI between four subgroups. However, no significant difference was observed in maximum and average heart rate between OSA and simple snoring patients.

## Correlation Between Peripheral Blood Cells with Clinical and Polysomnographic Parameters in Snoring Patients

Spearman or Pearson test was conducted to investigate the relationship between blood immune cells with clinical and polysomnographic parameters (Table 4). Monocytes were associated positively with COPD ( $r = 0.224$ ,  $P < 0.001$ ), smoking ( $r = 0.261$ ,  $P < 0.001$ ), AHI ( $r = 0.261$ ,  $P < 0.001$ ), the longest apnea duration ( $r = 0.181$ ,  $P = 0.002$ ), the sum of all desaturations ( $r = 0.169$ ,  $P = 0.005$ ), ODI ( $r = 0.194$ ,  $P = 0.001$ ) respectively, and negatively with average SpO<sub>2</sub> ( $r = -0.179$ ,  $P = 0.003$ ). Moreover, a significant correlation was observed between basophils and AHI ( $r = 0.12$ ,  $P = 0.046$ ) and ODI ( $r = 0.136$ ,  $P = 0.024$ ). The correlation analysis results for other blood parameters including WBC, neutrophils, lymphocytes, eosinophils, RBC, hemoglobin, platelets, NLR, PLR, and SII are presented in Table 4. The differences in peripheral blood immune cells in snoring patients with or without hypertension, COPD, and smoking are shown in Table 5.

## Risk Factors for Increased Peripheral Blood Monocyte and Basophil Count in Snoring Patients

In multiple linear regression, monocytes were independently associated with AHI ( $\beta = 0.314$ ,  $P = 0.005$ ), COPD ( $\beta = 0.15$ ,  $P = 0.029$ ), smoking ( $\beta = 0.189$ ,  $P = 0.004$ ), and maximum heart rate ( $\beta = 0.161$ ,  $P = 0.015$ ) (Table 6). However, there was no significance of the basophil's regression model (Table 7).

**Table 2** Peripheral Blood Immune Cells Expression in Snoring Patients

	Total (N=277)	Simple Snoring (N=81)	OSA (N= 196)	Mild (N= 80)	Moderate (N=46)	Severe (N=70)	P <sup>a</sup>	P <sup>*</sup>
<b>WBC (<math>\times 10^9/L</math>)</b>	6.5 (5.3–7.84)	6.49 (5.32–7.75)	6.5 (5.28–7.9)	6.1 (5.1–7.45)	6.4 (5–8.64)	6.56 (5.86–8.07)	0.819	0.459
<b>Neutrophils (<math>\times 10^9/L</math>)</b>	3.8 (3.02–4.8)	3.8 (3.15–4.63)	3.8 (2.9–4.81)	3.73 (2.9–4.4)	3.84 (2.8–5.32)	3.97 (3.02–5)	0.777	0.504
<b>Lymphocytes (<math>\times 10^9/L</math>)</b>	1.9 (1.43–2.3)	1.92 (1.6–2.43)	1.9 (1.4–2.3)	1.91 (1.4–2.23)	1.88 (1.38–2.23)	1.8 (1.4–2.24)	0.267	0.667
<b>Monocytes (<math>\times 10^9/L</math>)</b>	0.47 (0.4–0.6)	0.4 (0.31–0.5)	0.5 (0.4–0.62)	0.47 (0.4–0.6)	0.5 (0.38–0.64)	0.5 (0.4–0.69)	<b>&lt;0.001</b>	<b>0.001<sup>b</sup></b>
<b>Eosinophils (<math>\times 10^9/L</math>)</b>	0.125 (0.1–0.2)	0.1 (0.009–0.2)	0.14 (0.1–0.21)	0.1 (0.1–0.2)	0.175 (0.1–0.26)	0.16 (0.1–0.3)	0.127	0.087
<b>Basophils (<math>\times 10^9/L</math>)</b>	0.01 (0–0.0475)	0 (0–0.03)	0.02 (0–0.05)	0.01 (0–0.05)	0.02 (0–0.053)	0.02 (0–0.05)	<b>0.012</b>	<b>0.036<sup>c</sup></b>
<b>RBC (<math>\times 10^{12}/L</math>)</b>	4.59 (4.19–4.89)	4.7 (4.3–4.89)	4.55 (4.16–4.89)	4.47 (4.13–4.87)	4.46 (4.05–4.76)	4.67 (4.3–5.1)	0.145	0.029
<b>Hemoglobin (g/L)</b>	137 (127–148)	137 (124.5–147.5)	137.7 (128–149)	136.1 (129.1–145.8)	134.6 (124–146.8)	141 (130–154.6)	0.397	0.102
<b>Platelets (<math>\times 10^9/L</math>)</b>	228.5 (188.25–276)	238 (203–283.5)	226 (184–274.5)	238 (190–278)	227.5 (175.75–271)	217.5 (182.75–272.25)	0.175	0.337
<b>NLR</b>	2 (1.54–2.68)	2.06 (1.5–2.49)	2 (1.557–2.7)	1.94 (1.53–2.69)	2.05 (1.47–2.71)	2.05 (1.62–3)	0.375	0.669
<b>PLR</b>	126.78 (100–160.87)	125.52 (101.78–160.45)	127.35 (99.05–160.8)	129.6 (105–169.5)	128.22 (86.5–165.42)	125.12 (93.83–156.12)	0.889	0.649
<b>SII</b>	456.91 (357.75–635.67)	499.38 (359.87–620.52)	456.73 (353.77–666.58)	473.59 (366.36–625.45)	442.1 (332.78–695.04)	451.47 (348.7–667)	0.968	0.992

**Notes:** Data are presented as median (IQR). <sup>a</sup>P<sup>a</sup> indicates differences between simple snoring and OSA groups. <sup>\*</sup>The Kruskal–Wallis *H*-test (post hoc: Bonferroni). <sup>b</sup>Comparison between simple snoring and severe OSA group. <sup>c</sup>Comparison between simple snoring and moderate OSA. Bold values indicate statistical differences.

**Abbreviations:** WBC, white blood cells; RBC, red blood cells; NLR, neutrophils to lymphocyte ratio; PLR, platelet to lymphocyte ratio; SII, systemic inflammatory index.

**Table 3** Polysomnographic Parameters in Snoring Patients

	Total (N=277)	Simple Snoring (N=81)	OSA (N= 196)	Mild (N= 80)	Moderate (N=46)	Severe (N=70)	P <sup>a</sup>	P*
<b>AHI</b>	11.8 (3.7–30.75)	1.9 (0.65–3.1)	20.3 (11.05–38.4)	9.75 (7.1–12)	21.75 (18.9–24.43)	45.8 (36.28–61.63)	<b>&lt;0.001</b>	<b>&lt;0.001<sup>e</sup></b>
<b>The longest apnea duration</b>	36.65 (18.28–57)	12.7 (0–24.3)	40.9 (31–62.48)	32 (21.2–40.5)	39.5 (33.6–50.38)	63.55 (48.85–81.18)	<b>&lt;0.001</b>	<b>&lt;0.001<sup>e</sup></b>
<b>The sum of all desaturations</b>	103.5 (46–219.75)	34 (17.5–69.5)	158.5 (84.75–308.25)	85 (63–133)	138.5 (98–200)	329 (216–445.25)	<b>&lt;0.001</b>	<b>&lt;0.001<sup>e</sup></b>
<b>ODI</b>	14.95 (5.88–30.08)	4.8 (2.35–8.35)	21.1 (12.2–42.25)	12.2 (8.5–16)	21.85 (17.63–26.68)	46.35 (30.08–58.43)	<b>&lt;0.001</b>	<b>&lt;0.001<sup>e</sup></b>
<b>Minimum SpO<sub>2</sub> (%)</b>	79 (67–86)	85 (73.5–90)	77.5 (65–84.25)	83 (72–88)	78 (71.5–84.25)	68.5 (60–79)	<b>&lt;0.001</b>	<b>&lt;0.001<sup>b</sup></b>
<b>Average SpO<sub>2</sub> (%)</b>	95 (93.6–96)	96 (95–97)	94.4 (93–96)	95 (94–96.4)	94 (92.68–95.05)	93 (90.98–95)	<b>&lt;0.001</b>	<b>&lt;0.001<sup>b,c</sup></b>
<b>Maximum heart rate</b>	109 (99–116.75)	110 (100–120)	107 (98–116)	109 (99–117)	109 (104.75–116.5)	103 (95–114)	0.134	<b>0.04<sup>b</sup></b>
<b>Minimum heart rate</b>	51 (43–56)	53 (48–59)	49 (41–54)	50 (43–54)	50.5 (39–56.25)	48 (39.75–52.25)	<b>&lt;0.001</b>	<b>&lt;0.001<sup>b,c,d</sup></b>
<b>Average heart rate</b>	68.25 (63–75.28)	69.2 (62.8–75.1)	67.55 (63–75.3)	67.2 (62.3–74.5)	70 (65.45–77.48)	67.3 (63–75)	0.584	0.164

**Notes:** Data are presented as median (IQR). P<sup>a</sup> indicates differences between simple snoring and OSA groups. \*The Kruskal–Wallis *H*-test (post hoc: Bonferroni). <sup>b</sup>Comparison between simple snoring and severe OSA group. <sup>c</sup>Comparison between simple snoring and moderate OSA. <sup>d</sup>Comparison between simple snoring and mild OSA. <sup>e</sup>Comparison between simple snoring, mild, moderate, and severe OSA subgroups. Bold values indicate statistical differences.

**Abbreviations:** AHI, apnea-hypopnea index; ODI, Oxygen desaturation index.

**Table 4** Correlation Between Blood Immune Cells with Clinical and Polysomnographic Parameters in Snoring Patients

		WBC	Neutrophils	Lymphocytes	Monocytes	Eosinophils	Basophils	RBC	Hemoglobin	Platelets	NLR	PLR	SII
Age	r	<b>-0.306</b>	<b>-0.197</b>	<b>-0.493</b>	0.060	0.034	0.032	<b>-0.406</b>	<b>-0.269</b>	<b>-0.412</b>	<b>0.258</b>	<b>0.223</b>	0.015
	P	<b>&lt;0.001</b>	<b>0.001</b>	<b>&lt;0.001</b>	0.317	0.568	0.593	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>0.000</b>	<b>0.000</b>	0.800
BMI	r	<b>0.192</b>	<b>0.168</b>	<b>0.219</b>	-0.113	0.064	-0.025	<b>0.238</b>	<b>0.148</b>	<b>0.173</b>	-0.052	-0.107	0.036
	P	<b>0.001</b>	<b>0.005</b>	<b>&lt;0.001</b>	0.060	0.292	0.677	<b>0.000</b>	<b>0.013</b>	<b>0.004</b>	0.391	0.075	0.553
Hypertension	r	-0.122	-0.052	<b>-0.259</b>	0.051	0.032	0.117	<b>-0.142</b>	-0.094	<b>-0.307</b>	<b>0.166</b>	0.070	0.012
	P	0.051	0.403	<b>&lt;0.001</b>	0.415	0.604	0.060	<b>0.023</b>	0.130	<b>&lt;0.001</b>	<b>0.008</b>	0.261	0.842
Diabetes	r	0.014	0.066	-0.036	-0.004	-0.069	0.020	0.030	0.011	0.027	0.087	0.065	0.095
	P	0.825	0.296	0.570	0.950	0.277	0.756	0.630	0.856	0.671	0.165	0.304	0.132
COPD	r	-0.012	0.052	<b>-0.232</b>	<b>0.224</b>	0.047	0.009	-0.059	-0.018	-0.091	<b>0.208</b>	<b>0.149</b>	<b>0.136</b>
	P	0.853	0.415	<b>&lt;0.001</b>	<b>&lt;0.001</b>	0.457	0.885	0.357	0.773	0.152	<b>0.001</b>	<b>0.019</b>	<b>0.032</b>
Asthma	r	-0.074	-0.039	<b>-0.143</b>	0.050	0.081	-0.063	-0.026	-0.046	-0.062	<b>0.133</b>	0.102	0.080
	P	0.243	0.535	<b>0.024</b>	0.433	0.204	0.317	0.686	0.471	0.332	<b>0.035</b>	0.107	0.209
Smoking	r	0.089	0.099	-0.054	<b>0.261</b>	0.034	0.005	0.031	<b>0.176</b>	-0.065	<b>0.126</b>	0.050	0.101
	P	0.159	0.117	0.395	<b>&lt;0.001</b>	0.594	0.942	0.623	<b>0.005</b>	0.306	<b>0.045</b>	0.433	0.109
AHI	r	0.087	0.084	-0.050	<b>0.261</b>	<b>0.149</b>	<b>0.120</b>	0.027	<b>0.120</b>	<b>-0.118</b>	0.079	-0.043	-0.004
	P	0.149	0.163	0.407	<b>&lt;0.001</b>	<b>0.013</b>	<b>0.046</b>	0.650	<b>0.046</b>	<b>0.050</b>	0.190	0.478	0.942
The longest apnea duration	r	0.042	0.020	-0.004	<b>0.181</b>	<b>0.119</b>	0.060	0.039	0.115	<b>-0.125</b>	0.034	-0.067	-0.059
	P	0.483	0.746	0.509	<b>0.002</b>	<b>0.047</b>	0.322	0.517	0.055	<b>0.038</b>	0.573	0.268	0.328
The sum of all desaturations	r	<b>0.172</b>	<b>0.163</b>	0.058	<b>0.169</b>	0.081	0.141	<b>0.162</b>	<b>0.184</b>	-0.021	0.087	-0.071	0.062
	P	<b>0.004</b>	<b>0.006</b>	0.335	<b>0.005</b>	0.178	0.019	<b>0.007</b>	<b>0.002</b>	0.723	0.148	0.236	0.305
ODI	r	<b>0.158</b>	<b>0.154</b>	0.030	<b>0.194</b>	0.104	<b>0.136</b>	<b>0.138</b>	<b>0.170</b>	-0.024	0.102	-0.038	0.072
	P	<b>0.008</b>	<b>0.010</b>	0.614	<b>0.001</b>	0.084	<b>0.024</b>	<b>0.022</b>	<b>0.005</b>	0.697	0.089	0.528	0.233
Minimum SpO <sub>2</sub>	r	<b>-0.130</b>	<b>-0.139</b>	0.020	-0.045	-0.040	-0.038	-0.092	-0.020	-0.016	<b>-0.118</b>	-0.050	-0.117
	P	<b>0.030</b>	<b>0.021</b>	0.742	0.455	0.507	0.527	0.128	0.744	0.793	<b>0.050</b>	0.403	0.051
Average SpO <sub>2</sub>	r	<b>-0.153</b>	<b>-0.188</b>	0.021	<b>-0.179</b>	-0.045	-0.084	-0.042	-0.110	0.003	<b>-0.122</b>	-0.018	-0.117
	P	<b>0.011</b>	<b>0.002</b>	0.723	<b>0.003</b>	0.455	0.162	0.488	0.067	0.959	<b>0.042</b>	0.763	0.052
Maximum heart rate	r	<b>0.234</b>	<b>0.200</b>	<b>0.203</b>	0.011	-0.054	0.029	<b>0.190</b>	0.046	<b>0.287</b>	-0.027	0.022	0.141
	P	<b>&lt;0.001</b>	<b>0.001</b>	<b>0.001</b>	0.853	0.371	0.63	<b>0.002</b>	0.447	<b>&lt;0.001</b>	0.658	0.715	0.019
Minimum heart rate	r	0.007	0.035	-0.049	-0.085	-0.016	-0.039	0.030	-0.053	0.097	0.069	0.110	0.092
	P	0.902	0.558	0.415	0.157	0.796	0.514	0.622	0.384	0.109	0.249	0.068	0.128
Average heart rate	r	<b>0.275</b>	<b>0.255</b>	<b>0.142</b>	0.096	0.102	-0.005	<b>0.122</b>	-0.032	<b>0.239</b>	0.076	0.032	<b>0.183</b>
	P	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>0.018</b>	0.110	0.090	0.929	<b>0.044</b>	0.598	<b>&lt;0.001</b>	0.210	0.600	<b>0.002</b>

**Note:** Bold values indicate statistical differences.

**Abbreviations:** WBC, white blood cells; RBC, red blood cells; NLR, neutrophils to lymphocyte ratio; PLR, platelet to lymphocyte ratio; SII, systemic inflammatory index; BMI, body mass index; COPD, chronic obstructive pulmonary disease; AHI, apnea-hypopnea index; ODI, Oxygen desaturation index.

**Table 5** Peripheral Blood Immune Cell Expression in Snoring Patients with and without Clinical Comorbidities

	Hypertension		P	COPD		P	Smoking		P
	With (N=87)	Without		With (N=20)	Without		With (N=49)	Without	
WBC (× 10 <sup>9</sup> /L)	6.12 (4.78–7.39)	6.70 (5.60–7.90)	0.051	6.04 (4.79–8.40)	6.50 (5.30–7.80)	0.852	6.85 (5.60–8.49)	6.35 (5.28–7.70)	0.159
Neutrophils (× 10 <sup>9</sup> /L)	3.73 (2.80–4.43)	3.80 (3.10–4.80)	0.402	4.14 (2.88–5.61)	3.79 (3.01–4.68)	0.414	3.84 (3.29–5.25)	3.78 (2.90–4.57)	0.117
Lymphocytes (× 10 <sup>9</sup> /L)	1.65 (1.24–2.11)	2.00 (1.65–2.45)	<b>&lt;0.001</b>	1.43 (1.08–1.69)	1.91 (1.50–2.40)	<b>&lt;0.001</b>	1.90 (1.16–2.30)	1.90 (1.50–2.31)	0.394
Monocytes (× 10 <sup>9</sup> /L)	0.46 (0.39–0.63)	0.43 (0.40–0.60)	0.414	0.65 (0.45–0.83)	0.41 (0.39–0.60)	<b>&lt;0.001</b>	0.50 (0.43–0.73)	0.41 (0.37–0.58)	<b>&lt;0.001</b>
Eosinophils (× 10 <sup>9</sup> /L)	0.14 (0.10–0.25)	0.11 (0.10–0.20)	0.603	0.20 (0.10–0.23)	0.12 (0.10–0.20)	0.456	0.15 (0.10–0.27)	0.14 (0.10–0.20)	0.593
Basophils (× 10 <sup>9</sup> /L)	0.02 (0.00–0.05)	0.00 (0.00–0.04)	0.060	0.01 (0.00–0.05)	0.00 (0.00–0.04)	0.885	0.00 (0.00–0.05)	0.00 (0.00–0.04)	0.942
RBC (× 10 <sup>12</sup> /L)	4.39 (4.00–4.83)	4.59 (4.32–4.88)	<b>0.023</b>	4.26 (3.86–4.98)	4.56 (4.2–4.85)	0.356	4.55 (4.18–4.87)	4.57 (4.16–4.84)	0.622
Hemoglobin (g/L)	133.00 (123.98–147.33)	137.70 (129.30–147.00)	0.130	133.70 (124.80–148.75)	137.00 (126.63–146.88)	0.772	143.00 (133.70–152.70)	135.00 (125.00–145.05)	<b>0.005</b>
Platelets (× 10 <sup>9</sup> /L)	201.00 (170.00–242.75)	246.00 (207.00–286.00)	<b>&lt;0.001</b>	215.50 (177.25–233.25)	230.50 (188.00–277.00)	0.152	219.00 (191.50–260.50)	231.00 (187.75–279.00)	0.305
NLR	2.22 (1.57–3.30)	1.94 (1.53–2.41)	<b>0.008</b>	2.86 (2.25–4.55)	1.97 (1.52–2.47)	<b>0.001</b>	2.26 (1.62–3.02)	1.97 (1.52–2.47)	<b>0.045</b>
PLR	131.33 (98–171.25)	125.52 (99.64–158.50)	0.259	173.79 (107.86–211.01)	125.62 (98.69–158.55)	<b>0.019</b>	129.60 (95.70–181.11)	126.64 (99.18–158.75)	0.432
SII	463.79 (313.86–680.79)	465.95 (364.00–612.89)	0.841	609.72 (436.03–1076.48)	453.43 (351.28–622.41)	<b>0.032</b>	522.84 (356.97–697.59)	453.36 (349.81–617.13)	0.109

**Notes:** Data are presented as median (IQR). Bold values indicate statistical differences.  
**Abbreviations:** WBC, white blood cells; RBC, red blood cells; NLR, neutrophils to lymphocyte ratio; PLR, platelet to lymphocyte ratio; SII, systemic inflammatory index; COPD, chronic obstructive pulmonary disease.



**Table 6** Multiple Linear Regression Analysis for Peripheral Blood Monocyte Count in Snoring Patients

Variables	$\beta$	P	R <sup>2</sup>	P-value of Model
Age	−0.011	0.882	0.139	<0.001
BMI	−0.034	0.611		
AHI	<b>0.314</b>	<b>0.005</b>		
COPD	<b>0.150</b>	<b>0.029</b>		
Smoking	<b>0.189</b>	<b>0.004</b>		
The longest apnea duration	0.018	0.814		
ODI	−0.157	0.137		
Minimum SPO <sub>2</sub>	0.093	0.196		
Average SPO <sub>2</sub>	−0.131	0.096		
Maximum heart rate	<b>0.161</b>	<b>0.015</b>		
Minimum heart rate	0.022	0.724		

**Note:** Bold values indicate statistical differences.

**Abbreviations:** BMI, body mass index; AHI, apnea-hypopnea index; COPD, chronic obstructive pulmonary disease; ODI, Oxygen desaturation index.

**Table 7** Multiple Linear Regression Analysis for Peripheral Blood Basophil Count in Snoring Patients

Variables	$\beta$	P	R <sup>2</sup>	P-value of Model
AHI	−0.058	0.581	0.002	0.053
Asthma	−0.082	0.198		
Smoking	0.044	0.493		
The longest apnea duration	−0.039	0.631		
ODI	0.163	0.105		

**Abbreviations:** AHI, apnea-hypopnea index; ODI, Oxygen desaturation index.

## Discussion

OSA leads to various pathophysiological processes in the body such as sympathetic nervous system hyperactivity, oxidative stress, metabolic disorders, endothelial dysfunction, and airway inflammation, which causes systemic damage to multiple organs including immune dysfunction.<sup>19</sup> In our study, we investigated the differences in all peripheral blood immune cells and further analyzed risk factors for these differences in snoring patients of different severity. We found that the OSA patients had increased peripheral blood monocyte and basophil counts compared with simple snoring patients. Moreover, they increased gradually with the OSA severity. In addition, multiple linear regression analysis identified AHI, COPD, smoking, and maximum heart rate as independent predictors of monocyte count in OSA patients.

The level of blood monocytes is an indicator of the body's inflammatory state.<sup>20</sup> Sleep deprivation or restriction increases circulating monocytes and inflammatory cytokine production.<sup>21,22</sup> It was reported that the two fundamental pathophysiological mechanisms of OSA characterized by chronic intermittent hypoxia and sleep fragmentation interact with the immune system triggered by monocytes.<sup>23</sup> In addition, monocytes increase NLRP3 (NLR family pyrin domain containing 3) signaling under intermittent hypoxia conditions, leading to systemic inflammatory response.<sup>24</sup> Consistent with our results, a previous study demonstrated a positive association between monocytes and the severity of OSA measured by AHI.<sup>25</sup> At the same time, SpO<sub>2</sub> which considers the duration of intermittent oxygen desaturations was strongly and independently associated with specific inflammatory parameters including monocytes.<sup>26</sup> Besides, studies have demonstrated a positive correlation between basophils and the severity of OSA, which is consistent with our findings.<sup>25,27</sup> However, we did not find any risk factors for elevated basophils in OSA patients, possibly due to

insufficient sample size and data to analyze and draw correct conclusions. Thus, larger detailed investigations are needed to reveal the relationship between basophils and OSA in the future. Our findings suggest that intermittent hypoxia triggers systemic inflammation, leading to an increase in circulating monocytes. Therefore, peripheral monocyte count may be considered a valuable assessment tool for intermittent hypoxia in OSA.

COPD is a chronic airway inflammatory disease with persistent airflow obstruction due to exposure to inhaled particulate matter such as cigarettes and air pollutants.<sup>28</sup> COPD and OSA coexist and are accompanied by episodes in the same patient, defined as the “overlap syndrome”.<sup>23</sup> Patients with overlap syndrome experience a more significant reduction in nocturnal oxygen saturation and increased daytime hypercapnia compared to patients with either COPD or OSA alone.<sup>29</sup> These patients exhibit elevated levels of pro-inflammatory cytokines and reduced levels of anti-inflammatory cytokines resulting in a sustained state of chronic inflammation.<sup>30</sup> Therefore, more severe airway inflammatory states were observed in patients with overlap syndrome compared to those with COPD alone.<sup>31</sup> Likewise, a clinical study indicated that patients with overlap syndrome exhibit more severe endothelial damage, stronger inflammatory response, and lower cellular immune function.<sup>32</sup> Smoking can mobilize an increase in blood monocytes, which exacerbate inflammation in various diseases including chronic lung injury, tuberculosis, and ischemic brain injuries.<sup>33–35</sup> A systematic review showed that smokers have elevated levels of AHI and reduced minimum SaO<sub>2</sub> levels in OSA patients.<sup>36</sup> In brief, smoking leads to OSA development through various mechanisms, including airway inflammation, changes in sleep structure, unstable awakening mechanisms, and alterations in upper airway neuromuscular function.<sup>37,38</sup> Further, smoking increases systemic oxidative stress and inflammatory response.<sup>39</sup> In our study, COPD and smoking were independently associated with peripheral monocyte count, suggesting concomitant COPD exacerbates inflammation levels in OSA patients. Therefore, assessing COPD comorbidities and smoking status might be important for OSA patients’ inflammation levels in clinical practice.

In addition, our results showed that the maximum heart rate was associated with the monocytes. Hypoxemia and hypercapnia act on oxygen and carbon dioxide through peripheral and central chemoreceptors to increase the activity of the sympathetic nervous system in OSA.<sup>1</sup> Moreover, OSA patients experience elevated heart rate and muscle sympathetic activity during wakefulness, with further increases in blood pressure and sympathetic activity during sleep.<sup>40</sup> The heart rate also increases during inflammation situations. Thus, the maximum heart rate in OSA patients may also be related to systematic inflammation conditions. OSA patients can conveniently monitor their sympathetic nervous activity and inflammatory response during sleep by measuring their heart rate.

Lymphocytes also play an important role in inflammation and immune disease as executors of immune function.<sup>41</sup> Vicente E et al found increased CD4<sup>+</sup> T cells in pharyngeal lavage of OSA patients than those in controls.<sup>42</sup> In a previous study investigating phenotypic changes of various peripheral blood immune cells in patients with sleep apnea/hypopnea syndrome (OSAHS), significant differences were found in CD4<sup>+</sup> and CD8<sup>+</sup> T lymphocytes, CD19<sup>+</sup> B cells, and natural killer (NK) like T cells between OSAHS patients and control group. The authors also found the CD4<sup>+</sup>/CD8<sup>+</sup> T lymphocyte ratio is positively correlated with AHI and negatively correlated with the lowest SaO<sub>2</sub>. However, no significant difference was observed in the percentage of CD3<sup>+</sup> total T cells and dendritic cells between the OSAHS and control groups.<sup>43</sup> Consistent with our results, no significant differences were observed in peripheral blood total lymphocyte count. We will analyze the differential expression of peripheral blood lymphocyte subsets in OSA patients in further studies.

In addition, immune cell-driven inflammation is also associated with OSA and its severity. Increased IL-8 levels were observed in peripheral blood mononuclear cells supernatant of OSA children than in controls.<sup>44</sup> Likewise, a recent study involving different severe patients with OSA found that serum markers of high-sensitivity (hs)-CRP, TGF-β1, TNF-α, and IL-6 in OSA patients were significantly increased compared with normal controls.<sup>45</sup> However, Guasti L et al found that there was no difference in TNF-α releasing from peripheral blood mononuclear cells (PBMCs) and IL-8 produced by PMNs between OSA and control groups when similar prevalence of cardiovascular risk factors and cardio-metabolic therapies.<sup>46</sup> These differences may have occurred because only moderate and severe OSA patients with AHI greater than 20 were included in this study. Besides, the different statistical power and designs of these researches may also have influenced the final results. This may explain the differences in results between these studies and also highlights that future studies may take into account cardiovascular risk factors and cardiovascular treatments when exploring the role of cytokine imbalance and inflammation in OSA patients.

It was found that systemic inflammatory markers CRP, ESR, and NLR were correlated with OSA severity.<sup>47</sup> The SII, NLR, and PLR reflect the body's extensive immune and inflammatory states and have been used as new white blood-cell-based inflammatory indices in OSA. A cross-sectional study consistent with our results demonstrated that no significant difference was observed in the SII, NLR, and PLR between the different severe OSA subgroups. The further subgroup analysis showed a significant positive correlation between AHI and SII in the severe OSA subgroup.<sup>9</sup>

Our research has some limitations. Firstly, this study was a retrospective data analysis from a single center. The co-location of data collection and laboratory testing in a single hospital setting may lead to selection bias. Secondly, the sample size of OSA patients in our study was relatively small, which may limit the analysis and interpretation of the results. Thirdly, peripheral blood immune cell counts and polysomnography parameters from healthy subjects were absent. Therefore, further studies are required to validate the results in a more diverse and larger population.

## Conclusion

Our study showed that increased levels of blood monocyte and basophil counts were found in OSA patients compared with simple snorers. AHI, COPD, smoking, and maximum heart rate were risk factors for elevated peripheral blood monocyte count in OSA patients. These findings suggest that monocytes in peripheral blood could serve as an inflammatory biomarker for OSA, which contributes to a better understanding of hypoxia and systemic inflammation levels in OSA patients.

## Statement of Ethics

This study adhered to the Guidelines for Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) and complied with the tenets underlying the Declaration of Helsinki. This retrospective study was approved by the Ethics Committee of Zhongnan Hospital of Wuhan University (No.2023297K) and waived written informed consent from all patients. We have de-identified all patient information to protect the participants' privacy. The date of approval by the Ethics Committee was December 27, 2023.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare no conflicts of interest in this work.

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