

RESEARCH

Open Access



Hematological parameters as predictors of OSA severity

Rasha Mohamed Hendy¹, Basma M. Hani² and Salwa H. Mohammed^{1*}

Abstract

Background Obstructive sleep apnea syndrome (OSAS) is a common disease that has a prevalence of 6 to 13% of the adult population. It is characterized by recurrent obstruction partial or total upper airway and subsequent paroxysmal nocturnal hypoxia, leading to intermittent arousals from sleep and excessive daytime sleepiness.

This work aimed to evaluate the relationship between the hematological parameters in CBC with differential as a new biomarker showing systemic inflammation and as an indicator of OSAS severity.

Patient and methods This retrospective cross-sectional analysis included 100 subjects with OSA from those attending Chest departments in Benha University Hospital from 2021 to 2022 and 2022 to 2023 period. All patients were subjected to full history taking and clinical examination, electrocardiogram, chest X-ray posteroanterior view, full night of polysomnography, and complete blood count with differential.

Results There was a statistically significant difference between mild; moderate and severe OSA patients regarding platelets to lymphocyte ratio. A statistically significant difference between mild and severe OSA regarding neutrophil to lymphocyte ratio was found. There was a statistically significant positive correlation between OSA severity and platelet level, N/L, and P/L ratio.

Conclusion The hematological indices including neutrophil to lymphocyte ratio and platelet to lymphocyte ratio could be alternatives to expensive time-consuming biochemical markers to evaluate the inflammation and severity in the OSAS population.

Keywords Obstructive sleep apnea, Neutrophil lymphocyte ratio, Platelet lymphocyte ratio

Introduction

Obstructive sleep apnea syndrome (OSAS) is a popular disease with moderate to severe sleep apnea affecting 6 to 13% of adult persons [1]. It is recognized by recurrent partial or complete upper airway closure and subsequent paroxysmal nocturnal hypoxia, resulting in episodic sleep arousals and precipitous daytime sleepiness [2].

OSA could result in complications such as cardiovascular disorders (CVD) and diabetes [3]. And CVD includes

a large proportion of complications [4–6]. It is recognized that CVD complications of OSAS patients may be accompanied by endothelial dysfunction, exaggerated oxidative stress, systemic inflammation, and stimulation of the sympathetic system.

The chronic systematic inflammation of OSAS represents a crucial part of the evolution of CVD [12]. Recent research implies that both WBC and NLR are good indices of inflammation [13–17]. Neutrophils chiefly mediate innate immune response by secreting mediators while lymphocytes mediate adaptive immune response by regulating inflammation [18]. Also, some research showed that platelet was activated and aggregated in cases with OSAS, which was also important in inflammation [19, 20].

*Correspondence:

Salwa H. Mohammed
Salwa.has1986@gmail.com

¹ Departments of Chest Diseases, Benha University, Banha, Egypt

² Community Department, Benha University, Banha, Egypt

Recently, studies introduced PLR as a novel inflammatory marker to predict the adverse outcomes of CVD [14–17, 21]. It is found that HCT was increased in OSAS patients which might be called secondary erythrocytosis and this was suggested in view of the hypoxemic state [22]. Red cell distribution width (RDW), which assessed the variability of erythrocytes, was also reported to be increased in relation to inflammation in OSAS [23].

Patients and methods

This retrospective cross-sectional analysis included 100 patients with OSA from those attending Chest departments in Benha University Hospital from 1 January 2021 to 1 January 2023 period. Inclusion criteria included patients with diagnosed OSA by polysomnography and age equal to or more than 18 years. Exclusion criteria: patients known to have cardiovascular, renal, or hepatic diseases were excluded by history and laboratory (LFTs, KFTs). Patients with hematological disorders and malignancies were excluded by history. Patients diagnosed with obesity hypoventilation were excluded by ABG, complex sleep apnoea, central sleep apnea Cheyne-Stokes sleeping disorder, or REM-induced OSAS were excluded from the PSG results. Written consent was taken from all patients, and all of them were subjected to full history taking and clinical examination, Electrocardiogram. Chest X-ray posteroanterior view, CBC with differential leucocytic count, and a full night of polysomnography with a diagnosis of OSA severity by AHI using Somnoscreen plus PSG, Somnomdics, Germany. All those data were taken from the recordings in the sleep lab. All data were collected, tabulated, and statistically analyzed.

Statistical analysis

The statistical analysis was conducted using the Software, Statistical Package for Social Science, (SPSS Inc. Released 2009-PASW Statistics for Windows Version 26.0. Chicago: SPSS Inc.). All variables were tested for normality of distribution using the Shapiro–Wilk test. All *P* values were two-sided. Statistical significance was accepted at *p* value < 0.05. A *p* value > 0.05 was considered non-significant.

Results

The study population consisted of 100 patients divided into three groups according to disease severity (OSA classification) (mild: $5 \leq$ apnea–hypopnea index (AHI) < 15; moderate: $15 \leq$ AHI < 30; and severe: $30 \leq$ AHI). This article divided patients into three groups according to body mass index (BMI (normal weight: BMI < 25; overweight: $25 \leq$ BMI \leq 30; and obesity: $30 <$ BMI) (Table 1).

The median age (IQR) was 43 years [39, 51]. About 85% of the study cases were males and 15% were females.

Table 1 Baseline characteristics of cases (*N* = 100)

Variable		Statistics (<i>N</i> = 100)
Age (years)		
Median (Q1, Q3)	43 (39, 51)	
Age group	< 65 (<i>n</i> , %)	97 (97%)
	\geq 65 (<i>n</i> , %)	3 (3%)
Sex	Male (<i>n</i> , %)	85 (85%)
	Female (<i>n</i> , %)	15 (15%)
BMI ^a		
Median (Q1, Q3)	35 (31.3, 39)	
BMI classification	Normal weight (<i>n</i> , %)	5 (5%)
	Overweight (<i>n</i> , %)	16 (16%)
	Obesity (<i>n</i> , %)	79 (79%)
AHI ^a		
Median (Q1, Q3)	56.45 (35.35, 77.98)	
OSA classification ^a	Mild (5 to < 15) (<i>n</i> , %)	5 (5%)
	Moderate (15 to < 30) (<i>n</i> , %)	15 (15%)
	Severe (\geq 30) (<i>n</i> , %)	80 (80%)
DI ^a		
Median (Q1, Q3)	56.9 (29.85, 79.05)	

^a BMI Body mass index, AHI Apnea–Hypopnea Index, OSA Obstructive sleep apnea, DI Desaturation Index

Most patients (97%) were under 65 years of age. Median BMI (IQR) was 35 (31.3, 39). Seventy-nine patients (79%) were obese (BMI > 30) [35] compared with 16% overweight and 5% normal weight. Median AHI (IQR) was 56.45 (35.35, 77.98). Eighty patients (80%) reported a severe grade of AHI compared with 15% moderate and 5% mild. Median DI (IQR) was 56.9 (29.85, 79.05) (Table 1). We found that the median neutrophile count was 3.94 with IQR of (2.73, 5.33). The median lymphocyte count was 2.7 with IQR of (2.19, 3.25). Median platelet count was 247 with an IQR of (205, 291.25). Median HCT% was 46.85 with IQR of (44.2, 49.6). Median RDW-CV% was 12.03 with IQR of (11.3, 13.08). The median N/L ratio was 1.6 with an IQR of (1.1, 2.2). Median P/L was 94 with IQR of (80, 116.5) (Table 2).

Comparison between mild, moderate, and severe groups of OSA revealed that there were significant differences between the three groups regarding BMI, AHI, DI, and P/L ratio (*p* = 0.018, 0.001, 0.001, 0.024) respectively, where the severe OSA group recorded the greatest BMI (35.6 compared with 29 and 34), AHI (62.1 compared with 7.5 and 23.5), DI (65.7 compared with 13.8 and 22) and P/L ratio (95 compared with 63 and 95). There was a statistically significant difference between the mild and severe groups regarding the median N/L ratio (*p* = 0.041) (Table 3).

Spearman's correlation analysis showed that there was a statistically significant positive correlation between OSA

Table 2 Hematological indices of cases (N= 100)

Variable	Statistics (N= 100)
Neutrophile * 10 ⁹ Median (Q1, Q3)	3.94 (2.73, 5.33)
Lymphocyte 10 ⁹ Median (Q1, Q3)	2.56 (2.19, 3.25)
Platelet 10 ⁹ Median (Q1, Q3)	247 (205, 291.25)
HCT% Median (Q1, Q3)	46.85 (44.2, 49.6)
RDW-CV% Median (Q1, Q3)	12.05 (11.3, 13.08)
N/L ratio Median (Q1, Q3)	1.6 (1.1, 2.2)
P/L ratio Median (Q1, Q3)	94 (80, 116.5)

classification and BMI (rho=0.248, p=0.013), platelet level (rho=0.233, p=0.02), N/L ratio (rho=0.224, p=0.025) and P/L ratio (rho=0.218, p=0.03). No statistically significant correlation was detected between AHI and other parameters (p>0.05) (Table 4).

Univariate analysis by ordinal logistic regression revealed that BMI, platelets count, and P/L ratio were significant positive predictors for OSA classification (p=0.029, 0.048, 0.017) respectively (Table 5).

Discussion

In the current work, there was a statistically significant difference between the three groups of OSA severity regarding platelet to lymphocyte ratio, and there was a statistically significant difference between mild and severe OSA regarding median neutrophil to lymphocyte

ratio. There was a statistically significant positive correlation between OSA severity and platelet level, neutrophil to lymphocyte, and platelet to lymphocyte ratios, while the relation between OSA and other parameters (HT, RDW, –CV%, and neutrophils) was statistically nonsignificant. In the current study, univariate analysis by ordinal logistic regression revealed that platelets count, and P/L ratio were the most significant positive predictors for OSA severity (0.048, 0.017) respectively.

The chronic systematic inflammation of OSAS may play an important role in the progression of CVD [12]. Recent studies suggest that both WBC and NLR are good indicators of inflammation [13–17]. Neutrophils mainly mediate innate immune response by secreting mediators while lymphocytes mediate adaptive immune response by regulating inflammation [18]. Besides, some studies reported platelet was activated and aggregated in patients with OSAS, which was also relevant in inflammation [19, 20].

Many studies introduced PLR as a novel inflammatory marker to predict the adverse outcomes of CVD [14–17, 21]. In view of hypoxemic states, Choi et al. 2006 found that HCT was elevated in OSAS patients which might be called secondary erythrocytosis [22]. Ozsu, et al. 2012 reported that red cell distribution width (which assessed the variability of erythrocytes) was increased in relation to inflammation in OAS, this disagrees with our results, which show a nonsignificant correlation between OSA severity and both HCT and RWD [23].

Mindan et al. (2018) results showed that there was a positive correlation between the levels of hematological indices including (WBC, LYM, NLR, MPV, PDW, PLR, RDW, and HCT) and the severity of obstructive sleep apnea [23]. These results agreed with our work; which

Table 3 Comparison between the three groups according to OSA severity regarding age, BMI, DI, and hematological indices

Variable	Mild group (n= 5) Median (IQR)	Moderate group (n= 15) Median (IQR)	Severe group (n= 80) Median (IQR)	P value
Age	48 (40.5, 65)	40 (36, 47)	43 (39.25, 51.75)	P1 = 0.098, p2=0.054 p3=0.031, p4=0.075
BMI	29 (27.85, 32.1)	34 (29, 37)	35.6 (32.1, 40)	P1 = 0.018, p2=0.04 p3=0.01, p4=0.176
AHI	7.5 (7.15, 13.25)	23.5 (18, 26.7)	62.1 (50, 83.75)	P1 = 0.001, p2=0.001 p3=0.001, p4=0.001
DI	13.8 (4.45, 20.2)	22 (16.9, 27.2)	65.7 (49.23, 87.5)	P1 = 0.001, p2=0.049 p3=0.001, p4=0.001
Neutrophile	3.45 (2.91, 4.7)	3.46 (2.72, 4.55)	4.15 (2.71, 5.52)	P1 = 0.564, p2=0.97 p3=0.62, p4=0.32
Lymphocyte	3.5 (2.75, 3.57)	2.43 (2.13, 3.2)	2.56 (2.2, 3.2)	P1 = 0.145, p2=0.08 p3=0.054, p4=0.78
PLT	196 (190.5, 241)	219 (180, 293)	253.5 (208.8, 292)	P1 = 0.053, p2=0.66 p3=0.036, p4=0.13
HCT%	46.5 (36.55, 48.15)	46.8 (43.8, 50.7)	47 (44.2, 49.6)	P1 = 0.713, p2=0.51 p3=0.42, p4=0.83
RDW-CV%	12.8 (12.15, 15.9)	12.2 (11.2, 12.9)	12 (11.3, 13.3)	P1 = 0.328, p2=0.16 p3=0.15, p4=0.91
N/L ratio	1.2 (0.925, 1.35)	1.4 (1.1, 1.7)	1.75 (1.125, 2.3)	P1 = 0.058, p2=0.31 p3=0.041, p4=0.157
P/L ratio	63.4 (53.55, 87.5)	95 (75, 106)	95 (82.3, 123)	P1 = 0.024, p2=0.036 p3=0.009, p4=0.35

P1 comparison of the three groups using the Kruskal–Wallis’s test. P2 comparison between mild and moderate groups, using the Mann–Whitney U test. P3 comparison between mild and severe groups, using the Mann–Whitney U test. P4 comparison between moderate and severe groups, using the Mann–Whitney U test

Table 4 Correlation between OSA classification and other parameters ($n = 100$)

Parameters	Spearman's correlation coefficient (rho) value	P value
Age	0.085	0.399
BMI	0.248 ^a	0.013
Neutrophile	0.106	0.293
Lymphocyte	-0.083	0.409
Platelet	0.233 ^a	0.02
HCT%	0.027	0.762
RDW-CV%	-0.071	0.484
N/L ratio	0.224 ^a	0.025
P/L ratio	0.218 ^a	0.03

^a Correlation is significant at the 0.05 level (2-tailed). Spearman's correlation analysis showed that there was a statistically significant positive correlation between OSA classification and BMI ($\rho = 0.248, p = 0.013$), platelet level ($\rho = 0.233, p = 0.02$), N/L ratio ($\rho = 0.224, p = 0.025$), and P/L ratio ($\rho = 0.218, p = 0.03$). No statistically significant correlation was detected between AHI and other parameters ($p > 0.05$) as age, neutrophile, lymphocyte, and RDW-CV%

showed a positive correlation between OSA severity and platelets; platelet to lymphocyte and neutrophil to lymphocyte ratios. Mindan et al. (2018) proposed that these hematological indices could be alternatives to markers (like IL6 and CRP) to evaluate the inflammation in OSAS patients, which was useful for assessing the severity of OSAS [24].

The relationship between OSAS and accompanying changes in hematological parameters is complicated and can be explained by the following: acute and chronic hypoxia may be associated with MPV, PDW, and HCT changes. It was found that MPV and PDW were negatively related to average SpO₂ and minimum SpO₂ and implied that hypoxia could activate platelet function [19]. Rahangdale et al. (2011) demonstrated that a high level of oxygen desaturation was linked with higher platelet surface adhesion molecules, activated glycoprotein receptor expression, platelet-monocyte aggregation, and platelet-neutrophil aggregation. A hypoxemic state is interrelated with high hematocrit levels, as oxyhemoglobin desaturation can stimulate erythropoiesis, leading to increased hematocrit [25]. Svatikova et al. reported that ANP (atrial natriuretic

peptide) was increased overnight in those untreated OSAS patients, and ANP levels decreased with CPAP treatment. It indicated that hemoconcentration might lead to increased hematocrit [26]. Another mechanism appears to be sympathetic overactivity. It results in many pathophysiological changes such as recurrent arousals and increased inspiratory effort. OSAS patients exhibited high levels of sympathetic nerve activity even when they were fully awake, which contributed to platelet activation and CVD [27].

Larsson et al. (1989) suggested that platelet aggregability was increased by high levels of circulating catecholamine in vivo. Therefore, hematological indices associated with platelet activation (e.g., PLR) might change in OSAS patients caused by catecholamine discharge [28].

Some researchers declared that nuclear factor kappa B (NF- κ B), a master transcription factor that regulated the downstream inflammatory gene expression, was found to be selectively activated by hypoxia and reoxygenation [29]. NF- κ B activity also resulted in an increased number of circulating neutrophils and monocytes. And the apoptosis of neutrophils was dysregulated in the process of OSAS [30]. Both lead to elevated levels of neutrophils in the peripheral blood of OSAS patients. As for lymphocytes, OSAS patients combined with CVDs were found to have a lower lymphocyte level compared to those without CVDs, which could be due to the uncontrolled inflammatory pathway [31].

Moreover, some researchers demonstrated that lower lymphocyte counts were related to activation of the hypothalamus-hypophysis-adrenal (THA) axis, increased production of systemic cortisol levels, and altered sleeping habits [32]. The NLR, a novel marker of systemic inflammation, was associated with many chronic diseases and could be an indicator used to predict CVDs in OSAS patients [33]. On the other hand, many pro-inflammatory cytokines, such as IL6, could significantly promote the production and activation of platelets, which contributed to the changes in those hematological parameters including PLR, MPV, and PDW [34].

Table 5 Ordinal logistic regression for predictors associated with OSA classification

Variable	Estimate	Std. error	Wald	Df	Sig	95% confidence interval	
						Upper bound	Lower bound
BMI	0.098	0.045	4.77	1	0.029	0.010	0.186
PLT	0.01	0.005	3.91	1	0.048	-0.008	0.02
N/L ratio	0.758	0.402	3.56	1	0.059	-0.029	1.545
P/L ratio	0.027	0.011	5.66	1	0.017	0.005	0.05

Conclusion

The hematological indices including neutrophil to lymphocyte ratio and platelet to lymphocyte ratio could be alternatives to expensive time-consuming biochemical markers to evaluate the inflammation and severity in the OSAS population because they were comparatively cheap, readily measurable, easy, and practical laboratory markers.

Limitations

Small study size, not all hematological markers like MPV and PDW were included.

Abbreviations

OSA	Obstructive sleep apnea
ANP	Atrial natriuretic peptide
RDW	Red cell distribution width
THA	Hypothalamus-hypophysis-adrenal
HCT	Hematocrit
BMI	Body mass index
CVD	Cardiovascular disease
OSAS	Obstructive sleep apnea syndrome
N/L	Neutrophil lymphocyte ratio
P/L	Platelet lymphocyte ratio

Acknowledgements

The authors were grateful to all subjects who participated in this study.

Authors' contributions

Rasha wrote the discussion. Basma did the statistical analysis. Salwa collected data of the patients.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials

All data generated or analyzed during this study are included in this published article (and its Supplementary Information files).

Declarations

Ethics approval and consent to participate

The Research Ethics Committee of the Faculty of Medicine, Benha University, approved the protocol. Written consent was obtained from the patient's guardians. The reference number is RC 16–5-2023.

Consent for publication

Nothing to declare.

Competing interests

The authors declare that they have no competing interests.

Received: 14 September 2023 Accepted: 26 November 2023

Published: 10 January 2024

References

- Peppard PE, Young T, Barnett JH et al (2013) Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol* 177:1006–1014
- American Academy of Sleep Medicine. *International Classification of Sleep Disorders*. 3rd ed. IL (2014): American Academy of Sleep Medicine.
- Dewan NA, Nieto FJ, Somers VK (2015) Intermittent hypoxemia and OSA: implications for comorbidities. *Chest* 147:266–274
- Marin JM, Carrizo SJ, Vicente E et al (2005) Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *Lancet* 365:1046–1053
- Peker Y, Hedner J, Norum J et al (2002) Increased incidence of cardiovascular disease in middle-aged men with obstructive sleep apnea: a 7-year follow-up. *Am J Respir Crit Care Med* 166:159–165
- Dempsey JA, Veasey SC, Morgan BJ et al (2010) Pathophysiology of sleep apnea. *Physiol Rev* 90:47–112
- El Solh AA, Akinnusi ME, Baddoura FH et al (2007) Endothelial cell apoptosis in obstructive sleep apnea: a link to endothelial dysfunction. *Am J Respir Crit Care Med* 175:1186–1191
- Badran M, Ayas N, Laher I (2014) Cardiovascular complications of sleep apnea: role of oxidative stress. *Oxid Med Cell Longev* 2014:985258
- Jelic S, Padeletti M, Kawut SM et al (2008) Inflammation, oxidative stress, and repair capacity of the vascular endothelium in obstructive sleep apnea. *Circulation* 117:2270–2278
- Garvey JF, Taylor CT, McNicholas WT (2009) Cardiovascular disease in obstructive sleep apnoea syndrome: the role of intermittent hypoxia and inflammation. *Eur Respir J* 33:1195–1205
- Tamisier R, Pepin JL, Remy J et al (2011) 14 nights of intermittent hypoxia elevate daytime blood pressure and sympathetic activity in healthy humans. *Eur Respir J* 37:119–128
- Nadeem R, Molnar J, Madbouly EM et al (2013) Serum inflammatory markers in obstructive sleep apnea: a meta-analysis. *J Clin Sleep Med* 9:1003–1012
- Turak O, Ozcan F, Isleyen A et al (2013) The usefulness of neutrophil-to-lymphocyte ratio to predict in-hospital outcomes in infective endocarditis. *Can J Cardiol* 29:1672–1678
- Lattanzi S, Cagnetti C, Provinciali L et al (2017) Neutrophil-to-lymphocyte ratio and neurological deterioration following acute cerebral hemorrhage. *Oncotarget* 8:57489–57494
- Lattanzi S, Cagnetti C, Rinaldi C et al (2018) Neutrophil-to-lymphocyte ratio improves outcome prediction of acute intracerebral hemorrhage. *J Neurol Sci* 387:98–102
- Lattanzi S, Cagnetti C, Provinciali L et al (2016) Neutrophil-to-lymphocyte ratio predicts the outcome of acute intracerebral hemorrhage. *Stroke* 47:1654–1657
- Yu S, Arima H, Bertmar C et al (2018) Neutrophil to lymphocyte ratio and early clinical outcomes in patients with acute ischemic stroke. *J Neurol Sci* 387:115–118
- de Jager CP, van Wijk PT, Mathoera RB et al (2010) Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. *Crit Care* 14:R192
- Nena E, Papanas N, Steiropoulos P et al (2012) Mean Platelet Volume and Platelet Distribution Width in non-diabetic subjects with obstructive sleep apnoea syndrome: new indices of severity? *Platelets* 23:447–454
- Varol E, Ozturk O, Gonca T et al (2010) Mean platelet volume is increased in patients with severe obstructive sleep apnea. *Scand J Clin Lab Invest* 70:497–502
- Dotsenko O, Chaturvedi N, Thom SA et al (2007) Platelet and leukocyte activation, atherosclerosis, and inflammation in European and South Asian men. *J Thromb Haemost* 5:2036–2042
- Choi JB, Loreda JS, Norman D et al (2006) Does obstructive sleep apnea increase hematocrit? *Sleep Breath* 10:155–160
- Ozsu S, Abul Y, Gulsoy A et al (2012) Red cell distribution width in patients with obstructive sleep apnea syndrome. *Lung* 190:319–326
- Moher D, Liberati A, Tetzlaff J et al (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 6:e1000097
- Rahangdale S, Yeh SY, Novack V et al (2011) The influence of intermittent hypoxemia on platelet activation in obese patients with obstructive sleep apnea. *J Clin Sleep Med* 7:172–178
- Svatikova A, Shamsuzzaman AS, Wolk R et al (2004) Plasma brain natriuretic peptide in obstructive sleep apnea. *Am J Cardiol* 94:529–532
- Abboud F, Kumar R (2014) Obstructive sleep apnea and insight into mechanisms of sympathetic overactivity. *J Clin Invest* 124:1454–1457

28. Larsson PT, Hjemdahl P, Olsson G et al (1989) Altered platelet function during mental stress and adrenaline infusion in humans: evidence for an increased aggregability in vivo as measured by filtragometry. *Clin Sci (Lond)* 76:369–376
29. Ryan S, Taylor CT, McNicholas WT (2005) Selective activation of inflammatory pathways by intermittent hypoxia in obstructive sleep apnea syndrome. *Circulation* 112:2660–2667
30. Dyugovskaya L, Polyakov A, Lavie P et al (2008) Delayed neutrophil apoptosis in patients with sleep apnea. *Am J Respir Crit Care Med* 177:544–554
31. Altunayoglu Cakmak V, Ozsu S, Gulsoy A et al (2016) The significance of the relative lymphocyte count as an independent predictor of cardiovascular disease in patients with obstructive sleep apnea syndrome. *Med Princ Pract* 25:455–460
32. Acanfora D, Gheorghide M, Trojano L et al (2001) Relative lymphocyte count: a prognostic indicator of mortality in elderly patients with congestive heart failure. *Am Heart J* 142:167–173
33. Uygur F, Tanriverdi H, Aktop Z et al (2016) The neutrophil-to-lymphocyte ratio in patients with obstructive sleep apnoea syndrome and its relationship with cardiovascular disease. *Heart Lung* 45:121–125
34. Norol F, Vitrat N, Cramer E et al (1998) Effects of cytokines on platelet production from blood and marrow CD34+ cells. *Blood* 91:830–843
35. Centers for Disease Control and Prevention. About Child and Teen BMI. 2018. Accessed at www.cdc.gov/healthyweight/assessing/bmi/childrens_BMI/about_childrens_BMI.html on June 3, 2020

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.