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ORIGINAL ARTICLE

Evaluation of Neutrophil-Lymphocyte Ratio and Platelet-Lymphocyte Ratio in Obstructive Sleep Apnea Patients

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ABSTRACT

Background: Obstructive sleep apnea (OSA) is a condition marked by recurrent total or partial collapses of the upper airway during sleep, which result in obstructive apneas, hypopneas, and/or respiratory effort-related arousals. The aim of the present study was to predict outcome of OSA surgery by Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR).

Methods: This clinical trial study included 24 adult patients with obstructive sleep apnea who conducted at Otorhinolaryngoloy Department of Zagazig University Hospitals. The patients' clinical and demographic data including age, sex, body mass index,predisposing factors and comorbid condition were noticed OSA and differential blood count were obtained before and after surgery.

Results: There is significant higher value of WBCs, Lymphocyte, Neutrophil of severe obstructive apnea compared to moderate obstructive apnea $p<0.05$ before treatment. There is significant lower value of PLT, PLR of severe obstructive apnea compared to moderate obstructive apnea $p<0.05$ before treatment. But there was insignificant change of WBCs, Lymphocyte, PLR $P>0.05$. Whereas WBCs, neutrophil, lymphocyte, PLT, NLR, PLR significantly improved after treatment severe obstructive sleep apnea patients. There is significant and inverse relation between Apnea hypopnea index with lymphocyte, PLT, age. There is significant and direct relation between Apnea hypopnea index with NLR, WBCs, neutrophil.

Conclusion: PLR could be considered a new inflammatory marker for inflammation in OSA patients, as it is a quick, cheap, and easily measurable property on routine CBC analysis.

Keywords: Obstructive Sleep Apnea; Neutrophil-Lymphocyte Ratio; Platelet-Lymphocyte Ratio

INTRODUCTION

Obstructive sleep apnea (OSA), a chronic inflammatory condition that affects 3%–9% of the general population, is defined by recurring episodes of partial or total upper airway blockage while sleeping [1].

A simple complete blood count (CBC) analysis of peripheral blood can be used to evaluate the neutrophil to lymphocyte ratio and the platelet to lymphocyte ratio. Cardiovascular illnesses, several gynaecological and gastrointestinal malignancies, and systemic inflammation all result in an increase in the neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR). In our opinion, changes in NLR and PLR values, which reflect an increase in systemic inflammation, can be employed as pertinent parameters in the assessment of OSAS when the role of inflammation in the pathophysiology of OSAS is taken into account [2].

The ratios of leukocyte types may play a role in the inflammatory response to chronic illnesses, according to several research. To the best of our knowledge, however, the neutrophil to lymphocyte ratio in individuals with obstructive sleep apnea has

not yet been studied. Individuals with obstructive sleep apnea have leukocyte function alterations that have been shown to cause systemic inflammation in an animal model. Based on this information, we hypothesized that patients with more advanced disease could have a greater neutrophil to lymphocyte ratio [3].

Recent attention has been focused on a few systemic inflammatory markers that can be detected by normal blood tests due to their widespread availability and low cost. Among these, the neutrophil-to-lymphocyte ratio (NLR) has been acknowledged as a trustworthy indicator of systemic inflammation with predictive value in several chronic diseases. This is probably because persistent systemic inflammation stimulates white blood cells as the disease progresses [4,5].

Therefore, this research aimed to determine the predictive relevance of platelet-lymphocyte and neutrophil-lymphocyte ratios in OSA patients following surgery. Also, to establish the association between OSAS, NLR, and PLR values.

METHODS

This clinical trial study included obstructive sleep apnea adult patients and conducted at Otorhinolaryngoloy Department of Zagazig University Hospitals. An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Written informed consent of all the participants was obtained. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: obstructive sleep apnea adult male patients before and after surgery. Middle age group (30-50). Symptoms suggestive of OSA (moderate-severe). Failed or inability to tolerate CPAP. Moderate, severe OSAs patients. BMI < 30kg/m2. Age, gender, body mass index, risk factors, and concomitant conditions were noted in the patients' clinical and demographic data. OSA and differential blood count were also obtained.

Patients were excluded if they had a history of cancer, a chronic inflammatory condition, an infection of any kind, diabetes mellitus, uncontrolled hypertension, any type of cardiac disease, renal failure, or liver dysfunction. Also were excluded if they had good results with CPAP. Female gender (hormonal effect hematological disease) and BMI > 30kg/m2 were also excluded.

All patients were subjected to preoperative evaluation, including full history taking, complete clinical examination, blood samples, differential WBCs, and polysomnography. Sleep surgery is not a standard surgery, but it's tailored to every patient according to level of collapse. For example: nose (septoplasty, turbenectomy); nasopharynx (adenoidectomy); palate (anterior palate-plasty); suspension palate-plasty (expansion pharyncgeoplasty); oropharynx (tonsillectomy); and larynex (epiglottectomy). Polysomnography and CBC were performed postoperatively in all patients. All patients who were surgically managed were observed preoperative and up to 3 months postoperative.

Statistical analysis:

All data were analyzed using IBM SPSS Statistics for Windows (Version 23.0. Armonk, NY: IBM Corp.2015). Quantitative data were expressed as the mean ± SD & median, and qualitative data were expressed as percentage. T-test, Mann Whitnney, Paired t test, Wilcoxon signed ranks test, Spearman correlation coefficient was used. All tests were two sided. P-value < 0.05 was considered statistically significant (S), and P-value ≥ 0.05 was considered statistically insignificant.

RESULTS

The present study included 24 adult patients diagnosed as having obstructive sleep apnea Patients. Their mean age was 41.08±5.02years with a range from 36 to 50 years. Mean BMI was 29.98±2.93 with a range from 26.3 to 36.8. There is no significant difference between moderate and severe obstructive sleeping apnea patients regard to their age and BMI (Table 1).

All studied parameters have been significantly improved after treatment, except there was insignificant change of NLR, PLR, after treatment (Table 2). There is significant higher value of WBCs, Lymphocyte, Neutrophil of severe obstructive apnea compared to moderate obstructive apnea p<0.05 before treatment. There is significant lower value of PLT, PLR of severe obstructive apnea compared to moderate obstructive apnea p<0.05 before treatment. There is no significant difference of NLR of severe obstructive apnea compared to moderate obstructive apnea p>0.05 before treatment. There is significant higher value of WBCs, Neutrophil, NLR, of severe obstructive apnea compared to moderate obstructive apnea p<0.05 after treatment. There is no significant difference of other parameters of severe obstructive apnea compared to moderate obstructive apnea p>0.05 after treatment (Table 3).

There is significant higher value of Apnea hypopnea index of severe obstructive apnea

compared to moderate obstructive apnea p<0.05 before treatment. There is no significant value of Apnea hypopnea index of severe obstructive apnea compared to moderate obstructive apnea after treatment P>0.05 (Table 4).

Neutrophil, PLT, NLR ratio have been significantly improved after treatment of moderate obstructive sleep apnea patients, P<0.05. But there was insignificant change of WBCs, Lymphocyte, PLR P>0.05. Whereas WBCs, neutrophil, lymphocyte, PLT, NLR, PLR significantly improved after treatment severe obstructive sleep apnea patients (Table 5).

There was insignificant change of Apnea hypopnea index in moderate obstructive sleep apnea patients before and after treatment p>0.05. While there is significant change of Apnea hypopnea index in severe obstructive sleep apnea patients before and after treatment p<0.05 (Table 6).

There is significant and inverse relation between Apnea hypopnea index with lymphocyte, PLT, age. There is significant and direct relation between Apnea hypopnea index with NLR, WBCs, neutrophil. There is no significant relation between Apnea hypopnea index with PLR, BMI of studied post treatment of obstructive sleep apnea patients (Table 7).

Table 1: Comparison age per years, BMI in obstructive sleep apnea patients before treatment according to its severity

Variables	Moderate OSA (n.5)	Severe OSA (n.19)	t	P
Age per years Mean ±SD	41±2.7	41.1±5.5	0.041	0.97
BMI Mean ±SD	33.2±4.9	29.1±1.4	1.82	0.14

t= student t test nonsignificant (p>0.05).

Table 2: Comparison WBCs, Neutrophil, Lymphocyte, PLT, NLR, PLR and Apnea hypopnea index in OSA patients before and after treatment and percent of improvement

Variables	Studied patients (n.24)		percent of improvement	Paired t	p
	pre	post			
WBCs Mean ±SD Median(range)	6.73±1.93 6.1(4.4-9.7)	5.99±1.92 5.2(4-9)	10.84	8.686	0.0001*
Neutrophil Mean ±SD Median(range)	4.05±1.54 3.65(2.4-6.5)	3.54±1.63 3.25(1.6-6.1)	12.45	4.12	0.0001*
Lymphocyte Mean ±SD Median(range)	2.437±0.65 2.3(1.6-3.5)	1.88±0.6 1.68(1.1-3.2)	22.94	3.479	0.002*
PLT Mean ±SD Median(range)	238.74±51.6 224 (171-338()	184.92±25 175.5162-259)	22.55	7.144	0.0001*
NLR Mean ±SD Median(range)	1.65±0.53 1.5(1-3)	1.97±1.08 1.75(0.7-4.8)	19.58	w 1.64	0.1
PLR Mean ±SD Median(range)	108.79±49.9 90 (59.7-211.2)	108.94±44.2 106.3(53.4-235.4)	0.14	w 0.54	0.59
Apnea hypopnea index Mean ±SD Median(range)	48.82±18.5 47.7(16.7-74.9)	34.13±16.4 37 (6.1-61.3)	30.08	w 2.94	0.003*

Paired t test of significant, w: Wilcoxon signed ranks test nonsignificant (p>0.05). *significant (p<0.05).

Table 3: Comparison WBCs, Lymphocyte, Neutrophil, PLT, NLR and PLR before and after treatment according to severity of obstructive sleep apnea.

Variables	Moderate OSA (n.5)		Severe OSA (n.19)		P1	P2
	pre	post	pre	post		
WBC s Mean ±SD	5.08 ±0.93	4.3±0.27	7.16±1.91	6.44±1.91	0.004	0.02*
Neutrophil Mean ±SD	2.82 ±0.44	1.96±0.5	4.37±1.58	3.96±1.58	0.001	U 0.01*
Lymphocyte Mean ±SD	1.72 ±0.16	1.93±0.3	2.62±0.6	1.86±0.66	0.0001	0.82
PLT Mean ±SD	281±78	185.4±15	227.63±37	184.79±27	0.037	0.96
NLR Mean ±SD	1.58 ±0.11	1.04±0.5	1.66±0.6	2.21 ±1.06	0.58	U 0.028*
PLR Mean ±SD	167.8 ±59.4	96.7 ±7.6	93.25±34.4	112.16±49.3	0.046	U 0.49

t t= student t test u=Mannwhitnney u test nonsignificant (p>0.05). *significant (p<0.05).
P1=Compare before Moderate OSA & severe OSA patients, P2=Compare after Moderate OSA & severe OSA patients

Table 4: Comparison Apnea hypopnea index before and after treatment according to severity of obstructive sleep apnea.

Variables	Moderate OSA (n.5)		Severe OSA (n.19)		P1	P2
	pre	post	pre	post		
Apnea hypopnea index Mean ±SD Median range	24.7 ±7.3 30 (16.7-30)	23.2±12.59 14 (14-37)	55.17±14.9 50 (36.5-74.9)	37.01±16.437 (6.1-61.3)	t 0.001*	U 0.095

t t= student t test u=Mannwhitnney u test nonsignificant (p>0.05). *significant (p<0.05).
P1=Compare before Moderate OSA & severe OSA patients, P2=Compare after Moderate OSA & severe OSA patients

Table 5: Comparison NLR and PLR in moderate and severe obstructive sleep apnea patients before and after treatment and percent of improvement

Variables	Moderate OSA n.5				Severe OSA n.19			
	pre	post	% improve	P1	pre	post	% improve	P2
WBC s Mean ±SD	5.08 ±0.93	4.3±0.27	15.4	.057	7.16±1.91	6.44±1.91	10.0	0.0001*
Neutrophil Mean ±SD	2.82 ±0.44	1.96±0.5	30.5	.0001*	4.37±1.58	3.96±1.58	9.4	0.0001*
Lymphocyte Mean ±SD	1.72 ±0.16	1.93±0.3	12.6	0.36	2.62±0.6	1.86±0.66	29.1	0.002*
PLT Mean ±SD	281±78	185.4±15	34	.026*	227.63±37	184.79±27	18.8	0.0001*
NLR Mean ±SD	1.58 ±0.11	1.04±0.5	33.9	.038*	1.66±0.6	2.21 ±1.06	33	0.008*
PLR Mean ±SD	167.8 ±59.4	96.7 ±7.6	42.4	.21	93.25±34.4	112.16±49.3	20.3	0.048*

P1=Compare before and after Moderate OSA P2=Compare before and after Severe OSA, significant (p<0.05).

Table 6: Comparison Apnea hypopnea index in moderate and severe obstructive sleep apnea patients before and after treatment and percent of improvement

Variable	Moderate OSA n.5				Severe OSA n.19			
	pre	post	% improve	P1	pre	post	% improve	P2
Apnea hypopnea index Mean ±SD Median range	24.7 ±7.3 30 (16.7-30)	23.2±12.59 14 (14-37)	6	.67 9	55.17±14.9 50 (36.5-74.9)	37.01±16.4 37 (6.1-61.3)	33	.0001

P1=Compare before and after Moderate OSA, P2=Compare before and after Severe OSA significant ($p<0.05$).

Table 7: Comparison Apnea hypopnea index in moderate and severe obstructive sleep apnea patients before and after treatment and percent of improvement

Variables	After treatment of obstructive sleep apnea patients	
	Post Apnea hypopnea index	
	r	p
Post Apnea hypopnea index	1	.
NLR	.707**	0.0001
PLR	0.093	0.665
WBC	.517**	0.01
Neutrophil	.506*	0.012
Lymphocyte	-.451 *	0.027
PLT	-0.626 **	0. 001
age	-.426 *	0.038
BMI	-.053	0.806

(r) correlation coefficient ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

DISCUSSION

Obstructive sleep apnea (OSA) is a condition that is characterised by repeated whole or partial collapses of the upper airway while you are sleeping, which cause obstructive apneas, hypopneas, and/or breathing effort-related awakenings [1].

Systemic inflammation has been considered as a crucial component in the aetiology of cardiovascular problems in OSA patients, despite the fact that the exact underlying mechanisms are not entirely understood. Therefore, understanding how inflammation works is essential for managing OSA [6].

Clinical hypoxia-reoxygenation events enhance the production of oxygen-derived free radicals, which in turn leads to both local and systemic inflammation. [7,8].

Both oxidative stress and systemic inflammation play a significant role in the pathophysiology of obstructive sleep apnea. Intermittent nocturnal hypoxemia, which results in a drop in oxygen levels followed by reoxygenation when breathing resumes, is one possible mechanism at play [9].

Numerous biochemical and hematological markers can be used to determine the level of systemic inflammation. Despite the discovery of novel disease-specific biomarkers. Blood neutrophil to lymphocyte ratio, the majority of which are time- and money-consuming, is a simple and dependable measure that may be determined from white blood cell count [10]. This ratio combines knowledge of two distinct immune pathways: the lymphocytes that represent the regulatory pathway and the neutrophils that are in charge of continuing inflammation [11].

The association between the NLR and OSA has been studied in the past, but the findings have been inconsistent and contentious [5,12].

NLRs have been found to be significantly higher in OSA patients as compared to control groups in some previous studies. These results may have been inconsistent for a number of reasons, including the study's methodology, statistical power, and population's genetic heterogeneity [13].

The purpose of this study is to use the neutrophil-lymphocyte ratio and platelet-lymphocyte ratio to predict the outcome of OSA surgery. To ascertain the predictive usefulness of platelet-lymphocyte and neutrophil-lymphocyte ratios in OSA patients following surgery. to assess the worth of PLR in OSA patients. to ascertain the relationships between OSA severity and the NLR.The study was conducted at the Otorhinolaryngoloy Department of Zagazig University Hospitals. Number of patients admitted with obstructive sleep apnea is 4 cases per month; a comprehensive sample will be taken as 24 cases through 6 months.

The present study included 24 adult patients diagnosed as having obstructive sleep apnea Patients. Their mean age was 41.08±5.02 years with a range from 36 to 50 years. Mean BMI was 29.98±2.93 with a range from 26.3 to 36.8. All studied parameters have been significantly improved after treatment, except there was insignificant change of NLR, PLR, after treatment.

In our study, 19 patients had severe obstructive sleeping apnea (79.2%) and 5 patients had moderate obstructive sleeping apnea (20.8%). There is no significant difference between moderate and severe obstructive sleeping apnea patients regard to their age and BMI. There is significant higher value of WBCs, Lymphocyte, Neutrophil of severe obstructive apnea compared to moderate obstructive apnea $p<0.05$ before treatment. There is significant lower value of PLT, PLR of severe obstructive apnea compared to moderate obstructive apnea $p<0.05$ before treatment. There is no significant difference of NLR of severe obstructive apnea compared to moderate obstructive apnea $p>0.05$ before treatment. There is significant higher value of WBCs, Neutrophil, NLR, of severe obstructive apnea compared to moderate obstructive apnea $p<0.05$ after treatment. There is no significant difference of other parameters of severe obstructive apnea compared to moderate obstructive apnea $p>0.05$ after treatment.

In the present study, there is significant higher value of Apnea hypopnea index of severe obstructive apnea compared to moderate obstructive apnea $p<0.05$ before treatment. There is no significant value of Apnea hypopnea index of severe obstructive apnea compared to moderate obstructive apnea after treatment $P>0.05$.

Neutrophil, PLT, NLR ratio have been significantly improved after treatment of moderate obstructive sleep apnea patients, $P<0.05$. But there was insignificant change of WBCs, Lymphocyte, PLR $P>0.05$. Whereas WBCs, neutrophil, lymphocyte, PLT, NLR, PLR significantly improved after treatment severe obstructive sleep apnea patients.

In our study, there was insignificant change of Apnea hypopnea index in moderate obstructive sleep apnea patients before and after treatment $p>0.05$. While there is significant change of Apnea hypopnea index in severe obstructive sleep apnea patients before and after treatment $p<0.05$.

In the present study, there is significant and inverse relation between Apnea hypopnea index with NLR, PLR, PLT, age. There is significant and direct relation between Apnea hypopnea index with lymphocyte.

In our study, there is significant and inverse relation between Apnea hypopnea index with lymphocyte, PLT, age.There is significant and direct relation between Apnea hypopnea index with NLR, WBCs, neutrophil. There is no significant relation between Apnea hypopnea index with PLR, BMI of studied post treatment of obstructive sleep apnea patients.

The high frequency of OSA and AD co-occurrence draws growing attention and feeds the need to investigate the underlying processes of OSA and AD. There are a number of pathways that may contribute to comorbidity, according to research. First of all, investigations on both humans and animals have demonstrated that intermittent hypoxia stimulates the sympathetic nervous system, and repeated awakenings during sleep will amplify this effect. As a result, the resistance of end-apneic arterial pressure increases repeatedly [14,15].

Sozer et al [16] also claimed that OSA and its severity may be significantly predicted by the inflammatory biomarker pentraxin-3. NLR is a well-known and trustworthy biomarker of systemic inflammation, suggesting a larger inflammatory load. It reflects two different but complimentary immunological pathways: nonspecific active inflammation by neutrophils and specific immune control by lymphocytes. The NLR may therefore be more reliable and stable than other inflammatory markers.

In contrast, the physiological inspiration pressure

in healthy persons ranges from 5 to 8 cmH2O. Changes in intravascular and extravascular pressure cause the aorta to experience a clear increase in transmural pressure and significant shear stress, which will lead to AD. Additionally, Bai et al [17] discovered that in OSA patients, blood inflammatory cytokines (IL-6 and TNF-) were inversely correlated with the tensile strength of the aortic medial fibers.

NLR and OSA appear to be strongly correlated in several earlier investigations. NLR was significantly higher in OSA patients than in controls and was higher in severe OSA patients, according to a meta-analysis of eleven trials with 2,259 eligible participants [18,19].

Al-Halawani et al [20] found the NLR value in OSA patients before and after mandibular advancement devices were used to treat them. They discovered that the NLR was larger in people with moderate to severe OSA than in people with mild OSA, and in the subsequent subgroup analysis, the group receiving the best treatment experienced a statistically significant drop in both the NLR and AHI.

Our study was limited in that the CPAP treatment only lasted for four weeks. For the duration of the study, participants were requested to refrain from engaging in additional physical activities. Activity questionnaires were used to assess participants' levels of physical activity. This was done to make sure that any changes in physiological indicators were not the result of increased physical activity.

CONCLUSION

Using the neutrophil-lymphocyte ratio, which can be calculated from a full blood count with differential, in conjunction with other markers, may assist in identifying people with severe OSA. Future studies are required to demonstrate a notable reduction in the N/L ratio with successful continuous positive airway pressure (CPAP) therapy.

To determine the degree of disease inflammation in OSA patients, novel biomarkers are required. Considering that PLR is a quick, affordable, and simple to measure characteristic on standard CBC analysis, it could be thought of as a new inflammatory marker for inflammation in OSA patients.

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