Research Article

Open Access

Can Monocyte to HDL Ratio be a new Marker for Severity of Obstructive Sleep Apnea Syndrome?

Aida Mahmoud Yousef and Jehan J. El-Jawhari

¹Assistant professor of chest medicine, Mansoura University, Egypt²Assistant professor of clinical pathology**ABSTRACT**

Background: This study aimed to investigate the relation of serum monocyte to serum HDL cholesterol ratio (MHR) with obstructive sleep apnea syndrome (OSAS).

A total of 62 patients with an apnea hypopnea index (AHI > 5) and excessive daytime sleepiness were included in this study as OSAS group. The individuals with (AHI) < 5/h were included in the study as controls. OSAS patients were compared with the control group for high density lipoprotein (HDL) levels, serum monocyte count, and monocyte to HDL ratio (MHR). Mild, moderate and severe OSAS subgroups were compared for the same parameters.

Results: MHR was 11.93 ± 6.52 in the control group while it was 14.87 ± 6.98 in OSAS group, with a statistically significant difference in between them ($p = 0.016$). The MHR were positively correlated with AHI and the minimum oxygen saturation ($p = 0.003$ and $p = 0.012$, respectively).

Conclusion: serum monocyte to serum HDL cholesterol ratio increased as OSAS severity increased. MHR is an easy and available biomarker. It can be used as a new marker for severity of OSAS.

***Corresponding author**

Aida Mahmoud Yousef, Assistant professor of chest medicine, Mansoura University, Egypt, E-Mail: aidayousef2020@yahoo.com

Received: November 07, 2020; **Accepted:** November 16, 2020, **Published:** November 28, 2020

Keywords: Serum Monocyte to Serum HDL Cholesterol Ratio, Sleep Apnea

Abbreviations**MHR:** serum monocyte to serum HDL cholesterol ratio**AHI:** apnea hypopnea index**OSAS:** Obstructive Sleep apnea syndrome**CVD:** cardiovascular disease**HDL-C:** High-density lipoprotein cholesterol**LDL:** low-density lipoprotein**Introduction**

There is a link between Obstructive Sleep apnea syndrome (OSAS) and cardiovascular disease (CVD). Monocytes secrete prooxidant and pro-inflammatory cytokines at the site of inflammation, so, they are considered as important cells in the inflammatory process. High-density lipoprotein cholesterol (HDL-C) protects the endothelial cells against the unwanted effects of low-density lipoprotein (LDL) and to inhibit oxidation of LDL molecules [1].

Recently, monocyte to HDL Ratio [MHR] has emerged as a new cardiovascular prognostic marker. However, the association between MHR and patients with OSAS is still under investigation [2-5].

The aim of this study was to investigate correlation of MHR, with severity of OSAS.

Material and Method

A prospective study was conducted between May 2017 and July 2019. A total of 62 patients who underwent overnight polysomnography (PSG) due to complaints of excessive daytime sleepiness, snoring and witnessed apnea were included in the study. The patients with an AHI < 5 was considered as the control group while the ones with an AHI > 5 with OSA symptoms were considered as the OSAS group. Eighteen patients were a control group.

Exclusion criteria included patients with cardiovascular diseases (CVDs), hypertensive patients, chronic liver disease, chronic lung disease, malignancies, acute infection, and patients on medications that might affect the lipid profile (e.g. adrenergic blockers, steroids).

All subjects underwent a full-night Polysomnographic (PSG) study (sleep screen recorder viasys company Germany). Briefly, electroencephalogram, electrooculogram and electromyogram, thoracic and abdominal respiratory excursions, breath sounds, nasal pressure, electrocardiogram and oxygen saturation were registered. Respiratory events were scored manually.

Patients were categorized according to their AHI scores into OSAS negative (control) group (AHI < 5 / h), mild (AHI > 5 / h), moderate (AHI: > 15 / h), and severe OSAS (AHI > 30 / h) groups, according to the American Academy of Sleep Medicine (AASM) task force criteria [6].

The following morning after polysomnography, fasting venous blood samples were collected after a fasting period of 12 h, and analyzed within 60 minutes after collection for LDL, HDL levels, triglyceride, cholesterol; and leukocyte, neutrophil, lymphocyte, monocyte counts. MHR was calculated by dividing the monocyte count to HDL level. Furthermore, mild, moderate, and severe OSAS subgroups were compared with the control group for these parameters.

Monocyte, HDL and Monocyte/ HDL were separately compared with minimum oxygen saturation, AHI, the time of sleep under 90 % oxygen saturation in OSAS patients.

Written consents were obtained from the patients and healthy controls and the protocol of this study was approved by the Institutional Research Board of our faculty.

Statistical Analysis

Statistical analysis was carried out using SPSS program, version 10.0. Variables with normal distribution were compared with the Student's t-test and for variables not showing normal distribution, the Mann-Whitney U test was used. Kruskal–Wallis test was used to compare the differences between the groups. Post-hoc analysis was done as pairwise comparisons. Spearman's correlation was used for relationship between AHI and MHR. Receiver operating characteristic (ROC) curve analysis was applied to determine the cutoff value for MHR use in OSAS diagnosis. A two-tailed p value of $p < 0.05$ was considered as statistically significant.

Results

The PSG results revealed that 18 individuals did not have OSAS (control group), and 62 patients had OSAS (OSAS group). The mean age of control group was 42.4 years while it was 44.67 years in the OSAS group. The control group consisted of 12 males (66.7 %) and 6 females (33.3 %). OSAS group consisted of 40 (64.5 %) males, and 22 females (35.5 %) with no statistical difference (table1).

Table 1: Demographic characteristics

	OSAS(62)	CONTROL (18)	P value
Gender: N(%)	MALE 40 (64.5 %) Female 22 (35.5 %).	Male 12 (66.7 %) Female 6 (33.3 %)	0.274
Age(mean ± SD)	44.67 ± 15.16	42.41 ± 17.17	0.363
BMI	31.15 kg/m ²	29.64 kg/m ²	0.123

Body mass index (BMI) in OSAS group was 31.15 kg/m², while it was 29.64 in the control group, with no significant difference between both groups (table1)

The mean HDL levels were 40.12 mg/dL in OSAS group, while it was and 47.25 mg/ dL in the control group. There was a significant difference between both groups ($p = 0.039$) table2.

Table 2: Lipid profile and monocytes values in patients with OSAS and controls

	OSAS group	Control group	P value
Cholesterol (mg/dL)	208.50 ± 31.82	203.74 ± 25.42	0.563
Triglyceride (mg/dL)	199.13 ± 120.32	142.36 ± 44.82	<0.001
LDL (mg/dL)	128.50 ± 32.51	132.71 ± 22.15	0.767
HDL (mg/dL)	40.12 ± 12.45	47.25 ± 12.53	0.039
Monocyte ((10 ³ /L)	567.04 ± 169.16	554.03 ± 156.00	0.138
Monocyte/HDL	14.87 ± 6.98	11.93 ± 6.52	0.016
Lymphocyte (/L)	2489.06 ± 693.42	2425.24 ± 556.77	0.024
2425.24 ± 556.77	4327.27 ± 1487.45	4215.53 ± 1064.60	0.072

LDL low-density lipoprotein, HDL high-density lipoprotein
Bold values are statistically significant ($p < 0.05$)

The triglyceride levels were significantly different between control and OSAS groups ($p < 0.001$) table2.

OSAS and control groups showed significant differences for mean lymphocyte ($p = 0.024$), while, there was no statistically significant difference as regard the mean neutrophil counts ($p = 0.072$) table2.

The mean monocyte count was 567.04 ± 169.16 10³/L in OSAS group, and 554.03 ± 156.00 10³/L in the control group, without any significant difference in between ($p = 0.138$).

MHR was 11.93 ± 6.52 in the control group while it was 14.87 ± 6.98 in OSAS group, with a statistically significant difference in between ($p = 0.016$). (table2)

There were significant differences for monocyte counts between mild, moderate and severe OSAS subgroup ($p < 0.001$). There were significant differences for Monocyte/HDL between mild, moderate and severe OSAS subgroup ($p < 0.001$) (table 3).

Table 3: Comparison of obstructive sleep apnea subgroups for laboratory parameters, and statistical analysis

	Mild OSAS	Moderate	Sever	P value
Cholesterol (mg/dL)	210.81 ± 40.08	216.97 ± 40.44	205.16 ± 38.63	0.012
Triglyceride (mg/dL)	207.22 ± 129.10	199.77 ± 148.84	202.10 ± 173.56	0.038
LDL (mg/dL)	129.54 ± 27.73	136.68 ± 19.84	128.22 ± 33.75	0.019
HDL (mg/dL)	46.31 ± 12.63	44.87 ± 12.65	43.45 ± 8.75	0.023
Monocyte ((10^3 /IL)	526 ± 168	623 ± 200	628 ± 179	<0.001
Monocyte/HDL	11.52 ± 5.87	14.70 ± 7.96	14.84 ± 6.72	<0.001

LDL low-density lipoprotein, HDL high-density lipoprotein
Bold values are statistically significant ($p < 0.05$)

The MHR were positively correlated with AHI and the minimum oxygen saturation ($p = 0.003$ and $p = 0.012$, respectively).

High AHI and minimum oxygen saturation were significantly correlated with low HDL ($p = 0.001$ and $p = 0.002$, respectively) (table 4).

Table 4: Correlations of polysomnographic parameters and monocyte, HDL, monocyte/HDL

p value	Monocyte	HDL	Monocyte/ HDL
AHI	0.013	0.001	0.003
Minimum oxygen saturation	0.056	0.002	0.012
Time\90 % oxygen saturation	0.073	0.067	0.026

Bold values are statistically significant ($p < 0.05$)

Discussion

Repetitive episodes of nocturnal apnea in OSAS patients result in sympathetic system activation and increase the oxidative stress, which also implicated in the pathophysiology of endothelial dysfunction [7].

It has been known that monocyte activation plays an important role in chronic inflammation, in which monocytes and differentiated macrophages can modulate inflammatory cytokines and tissue remodeling. Monocyte become adherent to the surface of the endothelial cells and extravasate into the damaged tissue, thereby, induce the production of several cytokines—including interleukin (IL)-1, IL-6 (potent inflammatory cytokines) and tumor necrosis factor- α . Thereafter, monocytes differentiate into the macrophages that ingest the oxidized LDL cholesterol and form dangerous foamy cells [8- 10].

Contrarily, HDL molecules have an anti-inflammatory effect. It inhibits extravasation of the monocytes. It counteracts the monocyte activation and promotes efflux of oxidized cholesterol from the macrophages. The reduced HDL levels promote monocyte activation, and increase the risk for inflammation [11].

The relationship between OSAS and MHR was first investigated by Atan et al. in 2017, and they concluded that MHR could be a predictive marker in OSAS [12]. In the current study, the value of MHR of the patients with OSAS was statistically highly significant than that of the control group. This coincides with the study of Tamaki et al. who demonstrated that monocyte counts were higher in patients with OSAS than in the control group [13]. In our study, monocyte count increases as the severity of OSAS increases. In a recent multicentre study by Inonu Koseoglu et al., it was determined that MHR, as a systemic inflammation marker, could predict cardiovascular disease in OSAS patients

[14]. In the same study, a relationship was found between MHR and OSAS severity.

Our results coincides with the results of Atan et al in 2017 who found also that MHR significantly increased as AHI increased, and minimum oxygen concentration decreased [12]. There was a positive correlation between MHR and the severity of OSAS.

Conclusion: MHR increased as OSAS severity increased. MHR is an easy and available biomarker and can be used as a new predictor for severity of OSAS.

Limitations of this study should be mentioned. First, few number of patients were included in this study. Second, we did not study MHR changes before and after CPAP treatment. Thus, a further prospective clinical trial with CPAP treatment is needed in the future.

References

1. Nadeem R, Singh M, Nida M (2014) Effect of obstructive sleep apnea hypopnea syndrome on lipid profile: a meta-regression analysis. J Clin Sleep Med 10: 475-489.
2. Rogacev KS, Zawada AM, Emrich I (2014) Lower Apo A-I and lower HDL-C levels are associated with higher intermediate CD14?? CD16? monocyte counts that predict cardiovascular events in chronic kidney disease. Arterioscler Thromb Vasc Biol 34: 2120-2127
3. Zhang Y, Li S, Guo YL (2016) Is monocyte to HDL ratio superior to monocyte count in predicting the cardiovascular outcomes: evidence from a large cohort of Chinese patients undergoing coronary angiography. Ann Med 48: 305-12.
4. Cetin MS, Ozcan Cetin EH, Kalender E (2016) Monocyte to HDL Cholesterol Ratio Predicts Coronary Artery Disease Severity and Future Major Cardiovascular Adverse Events

- in Acute Coronary Syndrome. *Heart Lung Circ* 25: 1077-86.
5. Ganjali S, Gotto AM, Jr., Ruscica M (2018) Monocyte to-HDL-cholesterol ratio as a prognostic marker in cardiovascular diseases. *J Cell Physiol* 233: 9237-46.
6. (1999) Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The report of an American Academy of Sleep Medicine Task Force. *Sleep* 22: 667-689.
7. Shamsuzzaman AS, Gersh BJ, Somers VK (2003) Obstructive sleep apnea; implications for cardiac and vascular disease. *JAMA* 290: 1906-1914.
8. Dursunog˘lu N, Dursunog˘lu D (2005) Obstructive sleep apnea syndrome, endothelial dysfunction and coronary atherosclerosis. *Tuberk Toraks* 53: 299-306.
9. Adedayo AM, Olafiranye O, Smith D (2014) Obstructive sleep apnea and dyslipidemia: evidence and underlying mechanism. *Sleep Breath* 18: 13-18.
10. Imhof BA, Aurrand-Lions M (2006) Angiogenesis and inflammation face off. *Nat Med*. 12: 171-172.
11. Murphy AJ, Woollard KJ, Hoang A (2008) High-density lipoprotein reduces the human monocyte inflammatory response. *Arterioscler Thromb Vasc Biol* 28: 2071-2077.
12. Atan D, Kundi FCS, ˆzkan KM, Dere H (2017) A New Predictor for Obstructive Sleep Apnea Syndrome: Monocyte to HDL Ratio. *Indian J Otolaryngol Head Neck Surg* 69: 142-6.
13. Tamaki S, Yamauchi M, Fukuoka A (2009) Nocturnal hypoxic stress activates invasive ability of monocytes in patients with obstructive sleep apnoea syndrome. *Respirology* 14: 689-694.
14. Inonu Koseoglu H, Pazarli AC, Kanbay A, Demir O (2018) Monocyte Count/HDL Cholesterol Ratio and Cardiovascular Disease in Patients With Obstructive Sleep Apnea Syndrome: A Multicenter Study. *Clin Appl Thromb Hemost* 24: 139-44.

Copyright: ˆ2020 Aida Mahmoud Yousef. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.