University of Thi-Qar Journal of Science (UTJsci)
E-ISSN: 2709-0256, P-ISSN: 1991-8690, Vol. 11, No. 2, Dec. 2024

Correlation between Myeloperoxidase and Interleukin-6 of Patients with Obstructive Sleep Apnea Syndrome in Thi-Qar Governorate

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Received: 2024-05-15, Revised: 2024-06-27, Accepted: 2024-07-19, Published: 2024-12-05

***Abstract*- This research aimed to detect the relationship between Myeloperoxidase (MPO) and Interleukin-6 (IL-6) in patients obstructive sleep apnea syndrome (OSAS). The present study has been conducted on a number of healthy people and patients. Group A: 84 patients Obstructive sleep apnea syndrome (mild, mod and sever) with high blood pressure [47 male, 37 female] and age range (40 - 65). Group B: control group, consist of 64 healthy people [33 male, 31 female] and age range (40 - 65). The findings from the current research indicated a notable rise in levels of serum MPO and serum IL-6 among patient groups when compared with the control group ($P \leqslant 0.05$). Results indicated that there was a positive correlation between MPO with IL-6 in patients with OSAS. OSA patients show high serum myeloperoxidase and serum interleukin-6 concentrations, which signal heightened systemic inflammation and oxidative stress. These factors, part of the pathogenesis of cardiovascular disease are important risk predictors to measure in OSA patients: this can be helpful for early diagnosis of the disease.**

***Keywords*— Obstructive sleep apnea, Interleukin-6, myeloperoxidase .**

I. INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is when partial or complete obstruction of the upper airway occurs during sleep, with interruption (apnea) or reduction (hypopnea) of airflow, followed by brief awakening leading to restoration of airway permeability in the upper airway. These apnea/hypopnea cycles repeat several times per hour, resulting in sleep that is fragmented and almost unrecoverable. Within the upper respiratory tract, the pharynx, particularly the oropharynx and hypopharynx, is the area most susceptible to obstructive processes leading to OSAS [1] . OSAS negatively affects the health and behavior of millions of adolescents worldwide. It is an independent risk factor for many diseases, including hypertension, heart failure, heart disease, cardiovascular events, and arrhythmias. Unfortunately, it is a common chronic disease that seriously affects patients' lives [2] . The relationship between OSA and cardiovascular comorbidities stands out as a point of interest. In OSA patients, the periodic collapse of the upper airway during sleep leads to chronic intermittent hypoxia, which is believed to foster cardiovascular disease by way of triggering oxidative stress and sympathetic activation plus systemic and vascular inflammation [3-5]. Research at present highlights two main areas: the connection between inflammatory biomarkers and the severity of OSA, and predicting cardiovascular events among patients with OSA [6].

Myeloperoxidase (EC 1.11.1.7) is predominantly found in the high levels of immune cells, like neutrophils, monocytes, and macrophages [7-8]. Monocytes and macrophages [9] are also production by other types of cells in the body. MPO is normally contained within cytoplasmic membrane-bound granules known as azurophilic granules, which are released into the extracellular field by dissociation or exocytosis during excitation [10]. The entire biochemical mechanism of neutrophil degradation is unknown, but oxidative stress plays a key role in the release of MPO from these cells [11].

Activated neutrophils, monocytes, and certain types of tissue macrophages release MPO during inflammatory processes; they make use of H2O2 to oxidize various substrates which includes halides like Cl^-, Br^-, and pseudohalides such as thiocyanate (SCN^-). Consequently this results in the production of hypohalous acids— namely hypochlorous acid ($HOCl^-$), hypobromous acid ($HOBr^-$), and hypothiocyanic acid (HOSCN). An action initiated at inflammation [12]. Myeloperoxidase can interact with various ions, atoms, and molecules among which include $HOCl^-$, hydroxyl radicals, singlet oxygen, ozone, chloramines, and aldehydes [13,14]. These types are strong oxidants, toxic to microorganisms under normal and controlled conditions, and play important roles in the immune system. On the other hand any excessive or uncontrolled production of these bioactive chemicals may result into cellular damage leading to many different diseases [12].

IL-6 belongs to the IL-6 cytokine family, which consists of cardiotrophin-1, oncostatin M, leukemia inhibitory factor, cardiotrophin-like cytokine, ciliary neurotrophic factor, as well as interleukins 11, 27, 30, and 31. They all exist in beta form with the binding of glycoprotein 130 (gp130). The receptors trigger intracellular signaling cascades which are often formed by homo- or heterodimers of gp130 along with

https://doi.org/10.32792/utq/utjsci/v11i2.1253

other cytokine receptors. All these receptors are only present as beta forms upon binding to glycoprotein 130 [15]. Intermittent hypoxia plus chronic sleep fragmentation cause adipose tissue inflammation leading to increased release of IL-6 [16,17]. This could also have an effect on endothelial cells through adipocyte-produced mediators like IL-6 that induce NF-κB-promoter-based dysfunction of endothelium [18].

II. MATERIALS AND METHODS

A. Design of study

The research was carried out at AL-Nasiriyah General Hospital in Thi-Qar, especially the Respiratory Diseases Unit and the clinical biochemistry laboratory in AL-Haboubi Teaching Hospital, as well as specialist clinics during the timeframe from 1/12/2022 to 1/11/2023. The study comprised a total of (148) individuals, with (64) being control subjects and (84) being patients.

This study has been conducted on all number of almost healthy people and patients. Group A :84 patients Obstructive sleep apnea syndrome (mild , mod, and sever) with high blood pressure [47 male , 37 female] and age range between (40 - 65) . Group B : control group, consist of 64 almost healthy people [33 male , 31 female] and age range between (40 - 65). Some control samples were collected from outside the hospital and others were from people accompanying the patients.

B. Collection of a blood sample

Bloodsamples were obtained post the PSG polysomnography recorded in the Respiratory Diseases Unit at Nasiriyah General Hospital . Approximately (5mL) of blood samples from both obstructive sleep apnea patients and control groups were collected and left to clot in plain disposable tubes at room temperature. The samples were then centrifuged at 3000 rotations per minute (rpm) for 10 minutes; thereafter, the serum samples were separated and preserved at (-20ºC) for future evaluation of biochemical parameters unless needed on an urgent basis.

Serum Myeloperoxidase levels were measured by a commercially available ELISA kit (Human Myeloperoxidase (MPO) ELISA Kit, Shanghai YL Biotech Co.,Ltd). The assay range from 0.1 to 30 ng/ml. Serum Interleukin 6 levels and were measured by a commercially available ELISA kit (Human Interleukin 6 (IL-6) ELISA Kit, Shanghai YL Biotech Co.,Ltd). The assay range from 2 to 600 ng/L.

C. Statistical Analysis

"Statistical analysis was performed using the statistical package for the social sciences version 23, and findings were reported in the (mean± standard deviation) format. All groups that were analyzed used the T-test to compare various parameters. P-values ($P \leqslant 0.05$) were taken into consideration".

III. RESULTS AND DISCUSSION

TABLE I. CHARACTERISTIC DATA FOR ALL STUDIED GROUPS SHOWN IN TABLE I.

Groups	NO	Age year mean± SD	BMI(Kg/m^2) mean± SD	Male/ Female. N	Smoker No/yes	
					Male	Female
Control	64	47.09±5.82	28.60±4.6	33/31	18/15	31/0
Patients	84	52.89±6.50	35.71±4.88	47/37	27/20	37/0

A. Myeloperoxidase level in OSAS patients and control group .

Patient groups have shown higher serum MPO levels than the control group: table (II) displays this difference significantly ($P \leqslant 0.05$).

TABLE II. SERUM MYELOPEROXIDASE (MPO) CONCENTRATIONS OF (CONTROL) AND(PATIENTS) GROUPS

Group		N	MPO concentration (ng/ml) mean± SD
Female	Patients OSAS	37	2.77±.59[a]
	Control	31	1.77±.42[b]
Male	Patients OSAS	47	3.01±.61[a]
	Control	33	1.71±.50[b]
LSD			0.51

Each value represents mean ± SD values with non-identical superscript (a , b or c …etc.) were considered significantly differences ($P \leq 0.05$). OSAS: Patients obstructive sleep apnea. LSD: Low significantly differences.

MPO is primarily secreted by activated neutrophils at the site of inflammation it's a pro-oxidative enzyme with inflammatory activities. MPO catalyzes synthesis of various oxidants leading to oxidative damage within the inflamed area; among its functions include involvement in LDL oxidation and promoting dysfunction in HDL through atherogenesis, pathways highly related to MPO activity [19]. Also playing a role in metalloproteinases activation which contributes to plaque instability facilitating susceptibility for rupture: recent investigations have shown higher myeloperoxidase levels correlate with greater CVD risks as well being signifiers of mortality independent from other factors among ACS patients[20-22] OSA events can also be triggered due to elevated MPO levels since increased activity has been reported as a predictive risk marker towards developing CHD cases along other cardiovascular events [20-23]. Thus, high MPO might act as potential trigger for atherogenesis plus adverse cardiovascular cases in OSA context.

Individuals with OSA are at higher risk of CVD. Development of atherosclerosis and CVD are closely related to an increase in systemic inflammation; a marker for risk of systemic inflammation as well as cardiovascular disease is MPO activity in the plasma for patients with OSA [24].

B. Interleukin 6 level in OSAS patients and control group.

Patient groups have shown higher serum IL-6 levels than the control group: table (III) displays this difference significantly ($P \leq 0.05$).

TABLE III. SERUM INTERLEUKIN 6 (IL-6) CONCENTRATIONS OF (CONTROL) AND(PATIENTS) GROUPS

Group		N	IL-6 concentration (ng/L) mean± SD
Female	Patients	37	19.42±7.57[a]
	Control	31	9.52±3.78[b]
Male	Patients	47	22.62±11.21[a]
	Control	33	8.08±3.77[b]
LSD			7.65

- Legend as in table (II)

"IL-6 is a pleiotropic cytokine with pro-inflammatory, anti-inflammatory, and immune modulating functions

on numerous cell and tissue types" [25]. The IL-6 plasma levels were found to be related with the death rate among patients suffering from unstable coronary artery disease and interestingly, it was also found that those men who appeared healthy that had increased risk for future myocardial infarction [26-27].

Vascular inflammation is initiated and promoted by IL-6 inflammatory marker [28]. This marker also plays a role in the cardiovascular morbidity related to OSAS [29]. Working as a multifunctional cytokine with various activities upon secretion, including T lymphocyte proliferation plus B lymphocyte differentiation and stimulation of immunoglobulin secretion [30]. It should be noted that IL-6 triggers bone resorption in collaboration with other agents [30].

The most extensively studied cytokine in non-immune tissues is IL-6, recognized as a pleiotropic or "endocrine" cytokine [32]. Inflammation-related cytokines such as IL-6 play a role in physiological sleep regulation among healthy individuals, closely tied to circadian secretory patterns [30]. There is a possibility that good night's sleep and health in the next day are associated with decreased IL-6 secretion [30], while increased secretion of this cytokine can be reason for excessive daytime sleepiness (EDS) plus fatigue [32- 33]. Here we note that EDS is a common complaint among patients with sleep disorders [34] and one of the most significant physiological consequences of OSAS [35]; likewise, a meta-analysis on studies evaluating levels of IL-6 among patients diagnosed with major depression found these levels to be significantly higher compared to controls [36].

C. Correlation between Myeloperoxidase and Interleukin 6

Results indicated that there was a negative correlation between Myeloperoxidase with IL-6 in patients with OSA Table (IV) .

TABLE IV. CORRELATION BETWEEN MYELOPEROXIDASE AND INTERLEUKIN 6

		Interleukin 6
Myeloperoxidase	Correlation (R)	0.454-
	Sig. P- value	0.000

IV. CONCLUSION

OSA patients show high serum myeloperoxidase and serum interleukin-6 concentrations, which signal heightened systemic inflammation and oxidative stress. These factors, part of the pathogenesis of cardiovascular disease are important risk predictors to measure in OSA patients. This can be helpful for early diagnosis of the disease.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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