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Original article

Association between Serum Uric Acid and Lactate Levels in Patients with Obstructive Sleep Apnea and Their Relation with Disease Severity

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Abstract

Background: Obstructive sleep apnea (OSA) is the most prevalent variation of sleep-disordered respiration. Recurrent compression of the upper airway during sleep, which results in oxygen desaturation and subsequent arousals from sleep, is the hallmark of OSA. **This study aimed to** determine the existence of a correlation between OSA and serum uric acid and lactate levels as potential indicators of tissue hypoxia, as well as their correlation with disease severity. **Methods:** This prospective cross-sectional study included 50 patients with sleep related breathing disorders who were attend at sleep study unit, Chest department at Benha University Hospital. **Results**: There was a significant positive correlation between serum uric level after sleep and apnea–hypopnea index (AHI) and OSA classification, lactate after sleep, Epworth sleepiness scale (ESS),and oxygen desaturation index. There was a significant negative correlation between serum uric level after sleep and mean SpO_2, lowest SpO_2 and total sleep time. There was a significant positive correlation between lactate level after sleep and AHI and OSA classification, ESS and oxygen desaturation index. There was a significant negative correlation between lactate level after sleep and mean SpO_2, lowest SpO_2 and total sleep time. The serum uric acid and lactate after sleep was significantly higher compared to before sleep ($P < 0.001$). **Conclusion:** There was a significant association between sleep-related breathing disorders, particularly OSA and increased levels of serum uric acid and lactate, suggesting tissue hypoxia as a potential mechanism in OSA severity.

Keywords: Serum Uric Acid, Lactate Levels, Obstructive Sleep Apnea, Disease Severity.

Introduction

Sleep-disordered breathing (SDB), which is characterized by upper-airway obstruction during sleep, was initially identified in the 1960s. A group of physio-pathologic conditions known as SDB are defined by an anomalous respiratory pattern during sleep. Other respiratory, nervous, cardiovascular, or endocrine diseases may coexist with these conditions, or they may be isolated. It is now widely recognized by the general public that SDB is a widespread condition that is either responsible for or contributes to a variety of issues, such as hypertension, fragmented sleep patterns, and traffic incidents [(1)].

Obstructive sleep apnea (OSA) is the most prevalent form of SDB [(2).] The upper airway is repeatedly constricted during sleep, resulting in oxygen desaturation and additional arousals from sleep. This is the defining feature of OSA [(3)].

Patients who had OSA syndrome typically exhibit excessive daytime sleep and insomnia, as well as noisy snoring. There are numerous risk factors for OSAS, such as male sex, obesity, a short neck, and upper respiratory tract abnormalities [(4)].

OSAS is a sleep respiratory disorder that has the potential to be fatal as a result of its propensity to induce recurrent episodes of nocturnal hypoxia and hypercapnia, as supported by clinical experience. Cerebrovascular disease, hypertension, diabetes mellitus, and coronary heart disease are potential complications of these episodes, which may also lead to sudden mortality at night [(5)].

The prevalence of OSAS in recent years has been estimated to be between 2% in women and 4% and 7.5% in men, according to data from several major community-based population studies. The prevalence of OSAS in adults is estimated to be between 3% and 5%, according to domestic epidemiological investigations [(6)].

When OSAS is diagnosed using the apnea–hypopnea index (AHI), nocturnal polysomnography (PSG) is the clinical standard, as per the American Association of Sleep Medicine (AASM) criteria. Modest (AHI <15), moderate (15≤ AHI <30), or severe (AHI ≥30) are the three categories into which OSAS is classified. Cardiovascular morbidity and mortality, including hypertension, heart failure, and stroke, will result from hypoxemia [(7)].

Apneas that are present in patients with OSAS lead to a tissue hypoxia and reduction in arterial oxygen saturation, which is followed by reoxygenation after the cessation of apneas. This hypoxic oxidative stress (HOS) evolution is linked to the multiple cycle of hypoxia/reoxygenation. The net degradation of ATP to ADP and AMP is the consequence of HOS, which impairs

ATP synthesis (ATP from ADP). This cascade results in the liberation of the intermediates of purine nucleotides, including adenosine, inosine, hypoxanthine, and xanthine. The biosynthesis of uric acid (UA) is facilitated by purine catabolic products[(8)].

The utilization of lactate is considerably impeded by the absence of ATP in a state of hypoxemia, which significantly impairs the gluconeogenic process in the liver (Cori cycle) and renal cortex. In the event of tissue hypoxia, hyperlactatemia and lactic acidosis occur. Therefore, hyperuricemia and hyperlactatemia are assessed as indicators of tissue HOS in OSA patients [(9)].

The aim of this study was to identify whether there is a correlation between OSA and serum UA and lactate levels, which are potential indicators of tissue hypoxia, and their correlation with disease severity.

Patients and methods

This prospective cross-sectional study was conducted on 50 patients with sleep related breathing disorders who were attend at sleep study unit, Chest department at Benha University Hospital from January 2024 to January 2025.

Each patient was asked to sign a document indicating their fully informed permission. An explanation of the study's goal and a secret code number were given to each patient. The Research Ethics Committee at Benha University's Faculty of Medicine gave their approval before the study could begin.

Inclusion criteria were patients of any gender above 18 years old diagnosed as OSA by polysomnography and should be conscious and able to cooperate with the study.

Exclusion criteria were any diseases that affect sleep architecture and serum uric acid and lactate levels (heart failure, renal failure and gout), any medications that affect serum uric acid and lactate levels: (thiazide and loop diuretics and aspirin), total sleep time < 4 hours and any other medical conditions that result in increased serum uric acid or lactate level.

All studied patients were subjected to the following: **Demographic data collection from each patient including** [age, gender, occupation, and demographic details], medical conditions: such as acromegaly, hypothyroidism and neuromuscular disorders, family history, lifestyle factors: alcohol consumption, smoking or sedative medications, obesity, daytime sleepiness, snoring (loudness: loud snoring is a hallmark of OSA and snoring patterns: assess the frequency and duration of snoring episodes), witnessed apneas, morning headaches, restless sleep, nocturia and cognitive impairment. **Physical examination including** [A general examination includes the measurement of height, weight, body mass index (BMI), signs of systemic diseases, vital signs (blood

pressure, heart rate, respiratory rate, and temperature), neck circumference, and waist-hip ratio (WHR).] oropharyngeal examination: (mallampati score, inspection of the oral cavity and examination of the nasal passages), cardiovascular examination: heart murmurs or other signs of cardiovascular disease and Neurological examination: any neurological deficits that may contribute to upper airway obstruction]. **Lab investigations including** [Complete blood count, renal function tests (serum urea and creatinine), liver function test (ALT and AST), arterial blood gases, blood glucose levels, Electrolyte balance, lipid profile (low density lipoprotein (LDL) level, cholesterol level, high density lipoprotein (HDL) level, and triglycerides) and thyroid function Tests].

The Cardio Polysomnography apparatus VIASYS Healthcare Sleep Screen Apnea Screen (Germany) was employed to conduct nocturnal polysomnography (PSG) on all patients for a duration of 6-8 hours. The PSG recorded the following parameters: electroencephalography, electrooculography, continuous pulse oximetry, anterior tibialis electromyography, submental electromyography, electrocardiography, thoracic and abdominal movements, and oronasal ventilation. Time spent in TST was recorded for patients who underwent PSG. A record was made of the percentage of (%TST) spent below 95%, 90%, and 85% of SaO2. The cessation of ventilation for a duration of 10 seconds or more is the definition of adult apnea. Hypopnea is defined as a minimal 30% reduction in ventilation for 10 seconds in response to a 4% decrease in oxygen saturation. In the presence of abdominal and thoracic movements, the diagnosis of OSAS was established when there were apneas or hypopneas that exceed five per hour of sleep [(10)].

Serum UA and lactate levels were determined using two peripheral arterial blood samples: one was collected prior to sleep, and the other was collected at the conclusion of polysomnography. UA was estimated in a plain glass vial and lactate was estimated in a fluorized tube after the blood was promptly conveyed to the biochemical laboratory. The serum UA and lactate was measured by spectrophotometry method and by percentage of change in UA and lactate calculated as: [(a−b)/b×100] where a is the change before sleep and b is the change after sleep.

OSA severity grading

The AHI is utilized by the AASM to classify the severity of OSA. Mild OSA is defined as an AHI of 5 to 15, moderate OSA as 15 to 30, and severe OSA as 30 or greater [(11)].

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Statistical analysis

For the statistical study, the tools provided by IBM (Armonk, NY, USA)'s SPSS v26 were utilized. The normality of the data distribution was confirmed

using histograms and the Shapiro-Wilks test. The results of the post hoc test analysis of variance (ANOVA) were shown for the quantitative parametric data as the mean and standard deviation (SD) [(12).] Data for the qualitative variables were presented as frequencies and percentages after a Chi-square test was run [(13)]. A statistically significant result was defined as a two-tailed P value less than 0.05. To find out how closely related two numerical variables were, we utilized Pearson correlation [(14)]. The link between one dependent variable and multiple independent factors was examined using multiple regression [(15)].

A perfect test was defined as one that extended from the bottom left corner to the top left corner and subsequently to the top right corner, based on the results of the receiver operating characteristic curve (ROC) study, which measured the precision and specificity of each test's diagnoses.The area under the curve (AUC) was used to evaluate the test's overall performance. An AUC more than 50% is considered good, while an AUC close to 100% is considered excellent [(16)].

Results

Baseline characteristics, comorbidities, clinical presentation, vital signs classification of OSA according to AHI and OSA scale and clinical examination of the studied patients were showed in **Table 1.**

Laboratory investigations, polysomnographic oxygen saturation parameters, blood gas analysis, serum UA and serum lactate of the studied patients were recorded. The SUA and lactate after sleep was significantly higher compared to before sleep (P <0.001) **(Table 2)**

There was an insignificant difference among the different degree of OSA regarding age, sex and nocturnal hypoxemia, Hb, HbA1C, FBG, triglycerides, total cholesterol, LDL, HDL, and daytime $PaCO_2$. In severe degree the AHI was significantly higher compared to mild and moderate (P<0.001, <0.001) and AHI was significantly higher in moderate degree compared to mild moderate (P<0.001).

The daytime PaO2 was significantly lower in severe degree compared to mild (P= 0.005) with no significant difference between mild and moderate and between moderate and severe degree. The Epworth sleepiness was significantly higher in severe degree compared to mild and moderate (P<0.001, <0.001) and was significantly higher in moderate degree compared to mild degree (P < 0.001). Serum UA and serum lactate after sleep were significantly higher in severe degree compared to mild and moderate (P < 0.05) with insignificant difference between the mild and moderate degree. The mean SpO2 and lowest SpO2 were significantly lower in severe degree compared to mild and moderate (P<0.05) and was significantly lower in moderate degree compared to

mild degree (P < 0.05). The stop bang score was significantly higher in moderate and severe degree compared to mild degree (P<0.001, <0.001) with insignificant difference between the moderate and severe degree. In severe degree the oxygen desaturation index and arousal index were significantly higher compared to mild and moderate (P < 0.05) with no significant difference between the mild and moderate degree. The TST was significantly lower in severe degree compared to mild and moderate (P < 0.001, 0.004 respectively) with no significant difference between the mild and moderate degree. **Table 3**

There was a significant negative correlation between serum uric level after sleep and lowest SpO2 (r= -0.683, P <0.001), mean SpO2 (r= -0.609, P<0.001) and TST (r= -0.341, P=0.015). There was a significant positive correlation between serum uric level after sleep and AHI (r= 0.679, P <0.001) and OSA classification (r= 0.343, P=0.014), lactate after sleep (r= 0.527, P <0.001), Epworth sleepiness scale (ESS), (r= 0.681, P <0.001), and oxygen desaturation index (r= 0.369, P <0.001). There was an insignificant correlation between serum uric level after sleep and the other parameters including age, sex, nocturnal hypoxemia, Hb, HbA1C, FBG, triglycerides, total cholesterol, HDL, LDL, arousal index, daytime PaO2, daytime PaCO2 and stop bang scale. There was a significant positive correlation between lactate level after sleep and AHI (r= 0.405, P = 0.003) and OSA classification (r=0.463, P<0.001), ESS (r= 0.455, P = 0.001) and oxygen desaturation index (r= 0.300, P = 0.034). There was a significant negative correlation between lactate level after sleep and mean SpO_2 (r= -0.342, P= 0.015), lowest SpO_2 (r= -0.401, P = 0.004) and TST (r= -0.697, P<0.001). There was an insignificant correlation between lactate level after sleep and the other parameters including age, sex, nocturnal hypoxemia, Hb, HbA1C, FBG, triglycerides, total cholesterol, LDL, arousal index, daytime PaO2, daytime PaCO2 and STOP BANG scale. **Table 4**

The multiple regression analysis showed that OSA classification, AHI, ESS, lactate after sleep, mean SpO_2, lowest SpO_2, oxygen desaturation index, arousal index, and TST were significant predictors for serum UA after sleep. The multiple regression analysis showed that OSA classification, AHI, ESS, SUA after sleep, mean SpO_2, lowest SpO_2, oxygen desaturation index, and TST were significant predictors for serum lactate after sleep. **Table 5**

AUC for serum UA of 0.696 can significantly predict the OSA severity (P=0.010), at cutoff value of >6.67 mg/dL with 78.95% sensitivity, 54.84% specificity, 51.7% PPV and 81.0 % NPV. Also, AUC for serum lactate of 0.729 can significantly predict the OSA severity (P=0.001), at cutoff value of >2.87 mmol/L with 94.74% sensitivity, 51.61% specificity, 54.5% PPV and 94.1% NPV. **Figure 1**

Table 1: Baseline characteristics, comorbidities, clinical presentation, vital signs classification of OSA, and clinical examination of the studied patients

		Total (n=50)
Age (years)	**Mean± SD**	46.16± 12.41
	Range	26-65
Sex	**Male**	36 (72%)
	Female	14 (28%)
Height (m)	**Mean± SD**	1.67± 0.05
	Range	1.6-1.75
Weight (Kg)	**Mean± SD**	92.38± 14.32
	Range	66-119
BMI (Kg/m^2)	**Mean± SD**	33.41± 5.58
	Range	21.55-44.24
	Comorbidities	
HTN		19 (38%)
DM		14 (28%)
Dyslipidemia		23 (46%)
	Clinical presentation	
Nocturnal hypoxemia	**Yes**	14 (28%)
	Vital signs	
HR (beat/min)	**Mean± SD**	83.28± 4.91
	Range	75-90
SBP (mmHg)	**Mean± SD**	137.6± 10.98
	Range	120-160
DBP (mmHg)	**Mean± SD**	76.6± 8.95
	Range	60-90
Classification of OSA	**Mild**	8 (16%)
	Moderate	22 (44%)
	Severe	20 (40%)
	Clinical examination	
AHI (events/hour)	**Mean± SD**	31.88± 18.59
	Range	11-68
Stop-bang score	**Mean± SD**	5.14± 2.27
	Range	0-8
Epworth Sleepiness scale	**Mean± SD**	15.12± 3.8
	Range	7-21

BMI: body mass index. HTN: Hypertension, DM: Diabetes mellitus. OSA: Obstructive sleep apnea. HR: Heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure. AHI: apnea-hypopnea index.

Table 2: Laboratory investigations, polysomnographic oxygen saturation parameters, blood gas analysis, serum uric acid and serum lactate of the studied patients

			Total (n=50)	
Hb (g/dL)		**Mean± SD**	13.44± 1.15	
		Range	11.5-15.5	
HbA1C (%)		**Mean± SD**	7.5± 0.67	
		Range	6.5-8.5	
FBG (mg/dL)		**Mean± SD**	108.96± 29.93	
		Range	80-179	
Triglycerides (mg/dL)		**Mean± SD**	210.98± 54.03	
		Range	121-302	
Total cholesterol (mg/dL)		**Mean± SD**	177.58± 41.11	
		Range	110-236	
HDL (mg/dL)		**Mean± SD**	52.78± 7.58	
		Range	40-65	
LDL (mg/dL)		**Mean± SD**	135.08± 19.56	
		Range	103-168	
Polysomnographic oxygen saturation parameters				
Mean SpO_2 (%)		**Mean± SD**	76.42± 8.8	
		Range	64-97	
Lowest SpO_2 (%)		**Mean± SD**	57.36± 10.49	
		Range	45-79	
Total sleep time (hrs.)		**Mean± SD**	7.34± 0.62	
		Range	6.23-8.28	
TST<90% (hrs.)		**Mean± SD**	2.0± 1.66	
		Range	0.02-5.49	
		Median (IQR)	1.61 (0.57 - 2.93)	
Oxygen desaturation index		**Mean± SD**	55.38± 34.27	
		Range	0-120	
Arousal index		**Mean± SD**	34.67± 13.98	
		Range	12.5-58.7	
Blood gas analysis				
Daytime PaO_2 (mmHg)		**Mean± SD**	79.26± 6.08	
		Range	70-92	
Daytime $PaCO_2$ (mmHg)		**Mean± SD**	40.98± 3.31	
		Range	36-46	
Serum uric acid (mg/dL)	**Before sleep**	**Mean± SD**	6.02± 0.27	**<0.001***
		Range	5-6.39	
	After sleep	**Mean± SD**	6.96± 0.5	
		Range	6.17-7.82	
	% Change	**Mean± SD**	15.78± 9.83	
		Range	2.66 - 44.20	
Serum Lactate (mmol/L)	**Before sleep**	**Mean± SD**	1.03± 0.02	**<0.001***
		Range	1-1.07	
	After sleep	**Mean± SD**	1.91± 0.2	
		Range	1.6-2.25	
	% Change	**Mean± SD**	46.24± 9.13	
		Range	35.93 – 95.24	

Hb: Hemoglobin, HbA1C: glycated Hemoglobin, FBG: fasting blood glucose, HDL: high density lipoprotein,LDL: low-density lipoproteins.SpO_2: Oxygen saturation, TST: total sleep time. PaO_2: Partial pressure of oxygen, $PaCO_2$: Partial pressure of carbon dioxide. *: statically significant P value ≤0.05

Table 3: Association between OSA degree and baseline characteristics, examination, laboratory investigations, and different parameters Epworth sleepiness scale, blood gas analysis and polysomnographic oxygen saturation parameters

	Mild (n=8)	Moderate (n=22)	Severe (n=20)	P value
Age (years)	44.50 ± 14.35	44.64 ± 11.68	48.50 ± 12.69	0.562
Sex **Male**	8 (100%)	15 (68.2%)	13 (65%)	
Female	0 (0%)	7 (31.8%)	7 (35%)	0.152
Nocturnal hypoxemia	2 (25%)	7 (31.8%)	5 (25%)	0.868
Examination				
AHI (events/hour)	8.3 ± 4.5	17.5 ± 3.5	53.1 ± 9.0	**<0.001***
	P2<0.001*, P2<0.001*, P3<0.001*			
Stop bang score	1.3 ± 1.3	6.0 ± 1.4	5.8 ± 1.7	**<0.001***
	P1<0.001*, P2<0.001*, P3= 0.942			
Laboratory investigations				
Hb (g/dL)	13.31 ± 1.06	13.41 ± 1.15	13.52 ± 1.23	0.908
HbA1C (%)	7.50 ± 0.80	7.53 ± 0.71	7.47 ± 0.61	0.952
FBG (mg/dL)	108.38± 22.71	99.36± 22.51	119.75± 36.48	0.213
Triglycerides (mg/dL)	219.4 ± 43.1	209.7 ± 55.7	209.1 ± 58.2	0.895
Total cholesterol (mg/dL)	159.75 ± 36.50	187.82 ± 37.77	173.45 ± 44.93	0.219
HDL (mg/dL)	53.62 ± 5.01	54.45 ± 7.7	50.6 ± 8.04	0.247
LDL (mg/dL)	125.63 ± 14.45	134.55 ± 21.84	139.45 ± 18.02	0.240
Serum uric after sleep (mg/dL)	6.42 ± 0.44	6.63 ± 0.36	7.47 ± 0.41	**<0.001***
	P1= 0.411, **P2<0.001*, P3<0.001***			
Lactate after sleep (mmol/L)	2.62 ± 0.74	3.10 ± 0.81	3.67 ± 0.69	**0.004***
	P1=0.289, **P2= 0.005*, P3= 0.049***			
Epworth sleepiness scale	9.00 ± 1.31	13.82 ± 0.85	19.00 ± 1.52	**<0.001***
	P1<0001*, P2<0.001*, P3<0.001*			
Blood gas analysis				
Day time PaO_2 (mmHg)	85.3 ± 5.6	78.6 ± 4.8	77.6 ± 6.3	**0.006***
	P1= 0.160, **P2= 0.005*,** P3= 0.834			
Day time $PaCO_2$ (mmHg)	43.1 ± 3.6	40.6 ± 3.2	40.5 ± 3.1	0.134
Polysomnographic oxygen saturation parameters				
Mean SpO2 (%)	91.50 ± 3.42	78.09 ± 4.21	68.55 ± 3.39	**<0.001***
		P1<0001*, P2<0.001*, P3<0.001*		
Lowest SpO2 (%)	75.38 ± 2.88	60.09 ± 4.53	47.15 ± 1.73	**<0.001***
		P1<0001*, P2<0.001*, P3<0.001*		
Oxygen desaturation index	36.38 ± 29.45	54.23 ± 24.52	77.85 ± 30.99	**0.002***
		P1=0.281, **P2= 0.003*, P3= 0.024***		
Arousal index	31.99 ± 13.75	31.22 ± 12.48	49.32 ± 12.19	**<0.001***
		P1=0.988, **P2=0.005*, P3<0.001***		
Total sleep time (min)	7.90 ± 0.35	7.49 ± 0.59	6.94 ± 0.48	**<0.001***
		P1= 0.149**, P2<0.001*, P3=0.004***		

AHI: apnea-hypopnea index, Hb: Haemoglobin, HbA1C: glycated Haemoglobin, FBG: fasting blood glucose, LDL: low-density lipoproteins, PaO_2: Partial pressure of oxygen, $PaCO_2$: Partial pressure of carbon dioxide, SpO2: Oxygen saturation, *: statistically significant P value ≤ 0.05, P1= Mild compared to Moderate, P2 = Mild compared to Severe, P3 = Moderate compared to Severe.

Table 4: Correlation between serum uric and lactate after sleep and different parameters

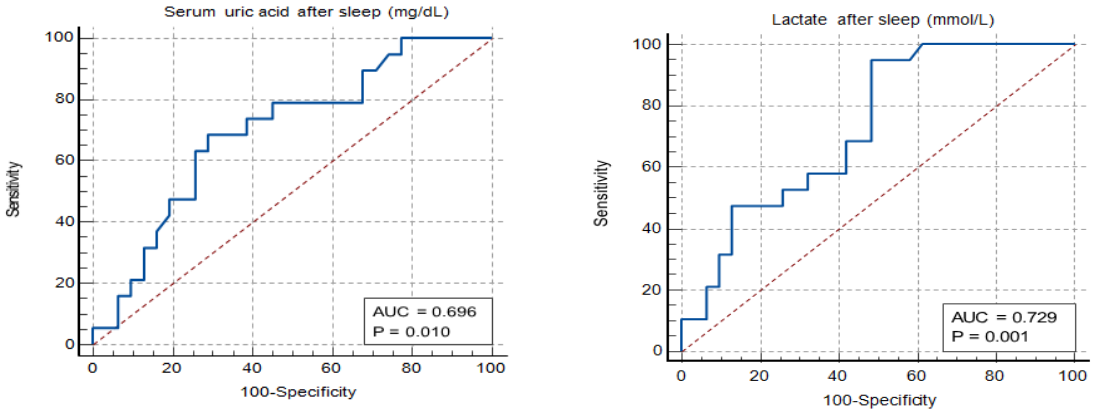
	Serum uric after sleep (mg/dL)		Lactate after sleep (mmol/L)	
	r	**P**	**r**	**P**
Age (years)	0.168	0.242	0.290	0.041
Sex	0.160	0.268	0.002	0.988
Nocturnal hypoxemia	0.087	0.549	0.093	0.520
Stop bang scale	0.260	0.068	0.154	0.285
AHI (events/hour)	0.679	**<0.001***	0.405	**0.003***
OSA classification	0.343	**0.014***	0.463	**<0.001***
Hb (g/dL)	0.226	0.115	0.288	0.043
HbA1C (%)	0.064	0.657	0.170	0.239
FBG (mg/dL)	0.127	0.805	0.055	0.706
Triglycerides (mg/dL)	-0.134	0.355	0.033	0.818
Total cholesterol (mg/dL)	0.024	0.870	0.191	0.184
HDL (mg/dL)	-0.098	0.500	0.111	0.443
LDL (mg/dL)	0.202	0.160	0.148	0.306
Lactate after sleep (mmol/L)	0.527	**<0.001***	---	---
Epworth sleepiness scale	0.681	**<0.001***	0.455	**0.001***
Mean SpO_2 (%)	-0.609	**<0.001***	-0.342	**0.015***
Lowest SpO_2 (%)	-0.683	**<0.001***	-0.401	**0.004***
Oxygen desaturation index	0.369	**0.008***	0.300	**0.034***
Arousal index	0.269	0.058	0.142	0.326
Total sleep time (hrs.)	-0.342	**0.015***	-0.697	**<0.001***
Day time PaO_2 (mmHg)	-0.168	0.244	-0.045	0.754
Day time $PaCO_2$ (mmHg)	-0.085	0.559	0.063	0.665

Hb: Haemoglobin, HbA1C: glycated Haemoglobin, HDL: high-density lipoprotein, LDL: low-density lipoproteins, SpO2: Oxygen saturation, OSA: Obstructive sleep apnea, PaO2: Partial pressure of oxygen, PaCO2: Partial pressure of carbon dioxide, AHI: apnea-hypopnea index, r: correlation coefficient, *: statistically significant P value ≤ 0.05.

Table 5: Multiple regression analysis for serum uric acid and lactate acid after sleep

	B	SE	T	P value
Serum uric acid				
Age (years)	0.005	0.011	0.475	0.637
Sex	0.544	0.309	1.758	0.086
BMI (Kg/m^2)	0.033	0.024	1.358	0.181
Nocturnal hypoxemia	0.040	0.311	0.129	0.898
OSA classification	0.643	0.170	3.783	**0.001***
Stop bang scale	-0.122	0.071	-1.718	0.093
AHI (events/hour)	0.013	0.006	2.240	**0.030***
Epworth sleepiness scale	0.123	0.037	-3.306	**0.002***
Uric acid after sleep (mg/dL)	0.589	0.244	2.416	**0.020***
Mean SpO_2 (%)	-0.023	0.007	-3.321	**0.002***
Lowest SpO_2 (%)	-0.018	0.009	-2.055	**0.045***
Oxygen desaturation index	0.008	0.004	2.105	**0.041***
Arousal index	-0.015	0.009	-1.639	0.108
Total sleep time (hrs.)	-0.475	0.197	-2.413	**0.020***
Day time PaO_2 (mmHg)	-0.017	0.022	-0.761	0.451
Day time $PaCO_2$ (mmHg)	-0.058	0.040	-1.463	0.150
Serum lactate acid				
Age (years)	0.005	0.011	0.475	0.637
Sex	0.544	0.309	1.758	0.086
BMI (Kg/m2)	0.033	0.024	1.358	0.181
Nocturnal hypoxemia	0.040	0.311	0.129	0.898
OSA classification	0.643	0.170	3.783	0.001*
Stop bang scale	-0.122	0.071	-1.718	0.093
AHI (events/hour)	0.013	0.006	2.240	0.030*
Epworth sleepiness scale	0.123	0.037	-3.306	0.002*
Uric acid after sleep (mg/dL)	0.589	0.244	2.416	0.020*
Mean SpO2 (%)	-0.023	0.007	-3.321	0.002*
Lowest SpO2 (%)	-0.018	0.009	-2.055	0.045*
Oxygen desaturation index	0.008	0.004	2.105	0.041*
Arousal index	-0.015	0.009	-1.639	0.108
Total sleep time (hrs.)	-0.475	0.197	-2.413	0.020*
Day time PaO2 (mmHg)	-0.017	0.022	-0.761	0.451
Day time PaCO2 (mmHg)	-0.058	0.040	-1.463	0.150

OSA: Obstructive sleep apnea, PaO2: Partial pressure of oxygen, PaCO2: Partial pressure of carbon dioxide, AHI: apnea-hypopnea index, SE: standard error, *: statistically significant P value ≤ 0.05.



A **B**

Figure 1: A: ROC curve analysis of serum uric acid for prediction of OSA severity, B: ROC curve analysis of serum lactate for prediction of OSA severity

Discussion

The present study revealed that according to demographic data in the studied patients, the age ranged from 26 to 65 years with a mean of 46.16± 12.41 years. There were 36 (72%) males and 14 (28%) females. The height ranged from 1.6 to 1.75 m with a mean of 1.67± 0.05 m, the weight ranged from 66 to 119 Kg with a mean of 92.38± 14.32 Kg and the BMI ranged from 21.55 to 44.24 Kg/m2 with a mean of 33.41± 5.58 Kg/m2.

These findings are in agreement with the objectives of Pıhtılı et al., who endeavored to examine the correlation between the severity of OSA and serum UA levels in patients with sleep-related respiratory disorders (SRBD). The study included 159 patients with SRBD. According to their report, the average age was 49.4±10.7 years. Males comprised 62% of the population, while females comprised 38%. The BMI was 38.7±4.2 kg/m2 [(17)].

Regarding the associated comorbidities, 19 (38%) patients had hypertension, 14 (28%) patients had diabetes mellitus, and 23 (46%) patients had dyslipidemia. Among the studied patients, 14 (28%) patients had a complaint of nocturnal hypoxemia.

These results in consistent with SÖkÜcÜ et al., who aimed to ascertain the correlation between serum UA concentrations and sleep parameters in patients with OSAS. They reported that 64 (57.1%) patients had hypertension, 32 (28.6%) patients had diabetes mellitus, and 24 (21.4%) patients had dyslipidemia [(18)].

According to AHI, there were 8 (16%) patients with mild OSA, 22 (44%) patients with moderate OSA and 20 (40%) patients with severe OSA. This came in accordance with SÖkÜcÜ et al. who reported that the OSAS group included 31 mild, 44 moderate and 37 severe cases of OSAS, grouped according to AHI value [(18)].

ESS ranged from 7 to 21 with a mean of 15.12± 3.8. The AHI ranged from 11 to 68 events/hour with a mean of 31.88± 18.59 events/hour. The Stop-bang score ranged from 0 to 8 with a mean of 5.14± 2.27.

In consistent with Elgazzar et al. who sought to determine the existence of a correlation between OSAS and both serum UA and lactate levels as potential indicators of tissue hypoxia, as well as their relationship with the severity of OSAS. They discovered that the AHI in OSA patients was modest in three patients, moderate in five, and severe in 12 patients. The AHI was within the range of 8.70–109.0 events/h, with a mean of 47.67±31.50 events/h. The mean of the ESS was 16.0±4.44, with a range of 8.0–22.0 (19).

In the current study, it was reported that the serum UA before sleep ranged from 5 to 6.39 mg/dL with a mean of 6.03± 0.27 mg/dL and after sleep ranged from 6.15 to 7.82 mg/dL with a mean of 6.92± 0.53 mg/dL. The % Change of serum UA ranged from -3.45 to 44.2% with a mean of 15.05± 10.73%. The serum UA after sleep was significantly higher compared to before sleep (P <0.001).

These findings in line with Elgazzar et al. who determined that the serum UA before sleep ranged from 5.50–6.80 mg/dL with a mean of 6.10±0.34 mg/dL and after sleep ranged from 5.90–7.90 mg/dL with a mean of 7.38±0.53 mg/dL. The serum UA after sleep was significantly higher than before sleep (P <0.001). The % Change of serum UA ranged from - 2.94– 33.90% with a mean of 21.01±8.16 **(19).**

In the current study, it was reported that serum lactate level before sleep ranged from 1-1.07 mg/dL with a mean of 1.03± 0.02 mg/dL and after sleep ranged from 1.88-4.47 mg/dL with a mean of 3.23± 0.78 mg/dL. The % Change of serum lactate ranged from 79.05 to 333.98% with a mean of 212.92±75.1. The lactate after sleep was significantly higher than lactate before sleep (P<0.001).

Similarly, the present study in agreement with Hira et al. whose findings indicated that the mean plasma lactate level of OSAS patients was 1.74 (±0.6) mmol/L before sleep and 2.28 (±0.98) mmol/L after sleep, both of which exceeded the standard laboratory reference value **(10).**

Regarding polysomnographic oxygen saturation parameters, the SpO2 ranged from 64 to 97 % with a mean of 76.42± 8.8 % and the lowest SpO2 ranged from 45 to 79 % with a mean of 57.36± 10.49 %. The total sleep time ranged from 6.23 to 8.28 hrs, with a mean of 7.34± 0.62 hrs, and the TST<90% ranged from 0.02 to 5.49 hrs, with a mean of 2.0± 1.66 hrs., the oxygen desaturation index ranged from 0 to 120 with a mean of 55.38± 34.27 and the arousal index ranged from 12.5 to 58.7 with a mean of 34.67± 13.98.

Similarly, the current study in agreement with Pıhtılı et al., who reported that mean SpO2 was 94.4±2.2% and the lowest SpO2 was 78.6±9.9%. The TST mean was 9.6±16.1hrs **(17).**

Regarding blood gas, it was found that the daytime PaO2 ranged from 70 to 92 mmHg with a mean of 79.26± 6.08 mmHg and the daytime PaCO2 ranged from 36 to 46 mmHg with a mean of 40.98± 3.31 mmHg. This came in accordance with Pıhtılı et al., who reported that the daytime PaO2 81.8±8.1

mmHg and the daytime PaCO2 41.6±2.2 mmHg [17].

In the current study, it was reported that there was an insignificant difference among the different degree of OSA and age, sex and nocturnal hypoxemia.

In consistent with Sunnetcioglu et al., who aimed to determine Patients with OSA exhibit elevated levels of SUA. They determined that there was no discernible distinction between the various degrees of OSA and the variables of age and sex [20].

In the current study, it was revealed that in severe degree the AHI was significantly higher than mild and moderate (P<0.001, <0.001) with no significant difference between the mild and moderate degree of OSA. The stop bang score was significantly higher in moderate and severe degree than mild degree (P<0.001, <0.001) with no significant difference between the moderate and severe degree of OSA.

Similarly, Sunnetcioglu and his colleagues reported progressive increase in the AHI was highly significant difference across the OSA groups, ranging from 9.2±3.1 in mild OSA, 21.5±4.0 in moderate OSA, and 57.6±24.1 in severe OSA, (p=0.001) [20].

In the current study, in severe degree SUA and serum lactate after sleep were significantly higher than mild and moderate (P < 0.05) with no significant difference between the mild and moderate degree.

In consistent with Shi et al. who discovered that the SUA levels were elevated in patients with OSAS (p < 0.01), particularly in those with severe OSAS (p < 0.01) [21].

The current study revealed that the daytime PaO_2 was significantly lower in severe degree than mild (P 0.005) with no significant difference between mild and moderate and between moderate and severe degree. ESS was significantly higher in severe degree than mild and moderate (P<0.001, <0.001) and was significantly higher in moderate degree than mild degree (P < 0.001).

This came in accordance with Jain et al. who There was a strong positive correlation between ESS (ESS) and AHI in patients with suspected OSA was analyzed. This suggests that a higher level of daytime sleepiness was associated with a higher number of respiratory events during sleep. There was statistically significant correlation between AHI and ESS. The AHI increased by 1.9 units for every 1-unit increase in ESS (p=0.021) [22].

In the current study, it was reported that the mean SpO_2 and lowest SpO_2 were significantly lower in severe degree than mild and moderate (P<0.05) and was significantly lower in moderate degree than mild degree (P < 0.05). The TST was significantly lower in severe degree than mild and moderate (P < 0.001, 0.004) with insignificant difference between the mild and moderate degree. The oxygen desaturation index and arousal index were significantly higher in severe degree than mild and moderate (P < 0.05) with insignificant difference between the mild and moderate degree.

These findings in line with Rezaie et al. who reported that individuals with severe OSA were had a lower SpO2, and

a lower TST, compared to individuals with mild or moderate OSA [23].

In the current study, it was found that there was a significant positive correlation between serum uric level after sleep and AHI and OSA classification, lactate after sleep, ESS, and oxygen desaturation index. There was a significant negative correlation between SUA level after sleep and mean SpO2, lowest SpO2 and TST.

These findings in line with Elgazzar et al. who determined significant positive correlation between SUA level after sleep study and AHI, %TST <90%, and ODI, whereas significant negative correlation with average and lowest SpO2% [19].

In the current study, it was reported that there was a significant negative correlation between lactate level after sleep and mean SpO2, lowest SpO2 and TST. There was a significant positive correlation between lactate level after sleep and AHI and OSA classification, Epworth Sleepiness and oxygen desaturation index.

These results in concordance with Elgazzar et al. who showed significant positive correlation between serum lactate level after sleep study and AHI, %TST <90%, and ODI, whereas significant negative correlation with average and lowest SpO2% was found [19].

The multiple regression analysis showed that OSA classification, AHI, ESS, lactate after sleep, mean SpO2, lowest SpO2, oxygen desaturation index, arousal index, and total sleep time were significant predictors for SUA after sleep.

These results in concordance with Pıhtılı et al., who reported that SUA levels were correlated with OSA severity, AHI, ODI and sleep time with SpO2 (17).

The multiple regression analysis showed that OSA classification, AHI, ESS, SUA after sleep, mean SpO2, lowest SpO2, oxygen desaturation index, and TST were significant predictors for serum lactate after sleep.

These findings in line with Elgazzar et al. who determined that AHI and ESS were significant predictors for serum lactate after sleep [19].

AUC for serum uric acid of 0.696 can significantly predict the OSA severity (P=0.010), at cutoff value of >6.67 mg/dL with 78.95% sensitivity, 54.84% specificity, 51.7% PPV and 81.0 % NPV. Also, AUC for serum lactate of 0.729 can significantly predict the OSA severity (P=0.001), at cutoff value of >2.87 mmol/L with 94.74% sensitivity, 51.61% specificity, 54.5% PPV and 94.1% NPV.

This came in accordance with Park et al. who revealed that individuals at high risk for OSA had higher SUA levels than those at low risk, with hyperuricemia independently associated with increased OSA risk [24].

Conclusion

From the findings of our study, it can be concluded that there was a significant association between sleep-related breathing disorders, particularly OSA and increased levels of SUA and lactate, suggesting tissue hypoxia as a potential mechanism in OSA severity. Higher levels of these biomarkers were found in patients with more severe OSA, making

them useful indicators of disease severity. Monitoring uric acid and lactate levels could help in evaluating OSA severity and understanding its underlying pathophysiology. Additional research is required to verify these discoveries and their clinical implications.

Future research should study the effect of medications and lifestyle regarding levels of serum uric acid and lactate, and how it can be useful in diagnosing and monitoring OSA severity.

This study has several limitations include small sample size, study design: as a cross-sectional study, it only looks at data from one point in time, making it difficult to establish relationships of cause and effect, the study didn't track patients over time, so it's unclear how changes in uric acid and lactate levels may affect OSA in the long term, single center: the study was conducted at one hospital, so the results may not apply to all patients with SRBD and there was not a comparison group of healthy individuals, which makes it hard to directly compare the biomarkers in OSA patients.

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