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AGMATINE, TELOMERASE AND TRACE MINERALS LEVELS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Obstructive sleep apnea syndrome (OSAS) is a disease characterized by repetitive, partially or complete upper airway obstructions resulting in hypoxia and bioelectrical wakefulness reactions along with sleep. There is a limited and different information on the biochemical pathways that may determine harmful effects in OSAS patients with different disease severity. Hence, we aimed to estimate the plasma levels of polyamine agmatine, which has many effects on the central nervous system, telomerase and trace minerals in patients with OSAS. The study included 90 volunteer patients diagnosed with OSAS and divided into three groups of 30 people each according to the apnea-hypopnea index (AHI) score: mild, moderate and severe. Nocturnal blood oxygen saturation percentage (SpO_2) and body mass index (BMI) were measured. Plasma agmatine level was defined by ultra-high-pressure liquid chromatography (UHPLC), plasma trace elements (Cu, Co, Mg, Mo, Zn, Se) level by inductively coupled plasma mass spectrometer (ICP-MS) and serum telomerase level by enzyme-linked immunosorbent assay (ELISA) method. It was found that SpO_2 value decreased as the disease progressed and showed a negative correlation with BMI, Co and Se plasma levels. The levels of agmatine and telomerase were shown to lower in patients with severe OSAS group compared to other groups.

K e y w o r d s: sleep apnea syndrome, agmatine, telomerase, trace minerals, SpO_2.

Obstructive sleep apnea syndrome (OSAS) is a common disease described as recurrent, complete (apnea), or partial (hypopnea) obstruction of the airway due to upper airway collapse during sleep. Immediately after this obstruction, oxygen saturation of hemoglobin decreases. Repeated cycles of hypoxemia caused by airway collapse have been associated with fluctuations in sympathetic activation, reactive oxygen species formation, increased inflammatory factors, and endothelial dysfunction [1]. The apnea/hypopnea index (AHI) indicates the severity of OSAS interpreted as the average number of apneas and hypopneas per hour [2].

Blood is a medium that provides the transport and collection of essential and toxic elements. Therefore, whole blood, plasma, and serum are suitable samples for the determination of a person's trace element status [3]. Trace elements, also known as micro minerals, are substances that take up less than 0.01% of the body mass and are of vital importance to be found in the body. Trace elements have very important functions for the human body. The daily requirements are different for each trace element. Taking these elements below daily requirements creates a sign of deficiency while taking them in excess creates a toxic effect [4]. It has been indicated that some immunological and inflammatory alterations can affect levels of trace elements in the body [5].

Agmatine is a biological polyamine formed by the removal of one mole of CO_2 molecule from the semi-essential L-arginine amino acid by the arginine decarboxylase enzyme (ADC). The biosynthesis of agmatine by ADC is dependent on the presence of L-arginine, which is a substrate for enzymes such as nitric oxide synthase (NOS) and arginase. L-arginine is converted to ornithine by arginase, while NOS catalyzes the conversion of nitric oxide (NO) and citrulline. The most important point of the agmatine molecule is an in vitro inhibitor of NOS and the progress of this reaction is competitive. Moreover, this effect was associated with the functional consequences of agmatine action in the brain [6]. It has been reported to have many effects, mostly on the central nervous system. It is also identified as a new neurotransmitter [7]. In addition, it has been reported that agmatine has some effects on the in-

sulin release from pancreatic islet cells, inhibition of vasopressin release, the release of adrenaline and norepinephrine, stimulation of gastrin secretion, and luteinizing hormone-releasing factor, and neuroprotective and neuromodulator missions [8].

Telomerase (EC 2.7.7.49) is a reverse-transcriptase structure of ribonucleoprotein belonging to a large family of enzyme complexes and is responsible for the synthesis of "TTAGGG" repeats at the chromosomal ends. Telomerase, which protects the integrity of the chromosome, takes part in tumor formation, aging, and cell division [9]. There are many studies on the shortening of telomerase in OSAS patients. In studies conducted with OSAS patients, it was found that patients had shorter telomeres than healthy controls [10, 11].

This information suggests that exposure to hypoxic conditions in OSAS may adversely affect trace element and agmatine levels by disrupting some biochemical pathways that may cause harmful effects. For example, hypoxia affects pathways such as the formation of reactive oxygen species, disruption of oxidant/antioxidant balance, the surge of sympathetic activation and, increased inflammatory factors and endothelial dysfunction. In addition, there is limited and different information on plasma trace element levels and no information about plasma agmatine levels in OSAS. For this reason, the objective of the study was to determine plasma trace elements and agmatine levels in OSAS patients of different severity, to assess whether these parameters reflect the severity of OSAS. In addition, we assessed various biochemical parameters, serum telomerase levels, BMI, SpO_2, and AHI values in patients with OSAS and examined the correlation of these parameters with demographic, and biochemical variables, and disease severity.

Material and Methods

Participants and ethical conditions. The study group consisted of 90 newly diagnosed OSAS patients who were admitted to the Clinic for Chest Diseases of the Research and Practice Hospital of Sivas Cumhuriyet University Faculty of Medicine between June 2019 and March 2021. For the definitive diagnosis of OSAS, the patients were hospitalized overnight in the Sleep Center and a polysomnography test was performed. OSAS patients, who were randomly selected without discrimination in terms of age and gender, were connected to the PSG (The Grass Technologies Product Group, USA) device for one night and various measurements were taken and the values were recorded. The apnea/hypopnea index (AHI) was defined as the sum of the apnea and hypopnea number per hour of sleep. Volunteer patients were grouped into three based on apnea-hypopnea index (AHI) scores: mild OSAS (n = 30; 5 ≤ AHI ≤ 13.7), moderate (n = 30; 15.8 ≤ AHI ≤ 26.6) and severe (n = 30; 34.1 ≤ AHI ≤ 86.3). The mean SpO_2 percentages of the PSG device were measured from the fingertip with a system-defined pulse oximeter. Demographic information and measurements such as height, weight, and BMI were obtained before PSG.

Approval for the study permission was obtained by Sivas Cumhuriyet University Clinical Research Ethics Committee (2018-12/02). In addition, written informed consent was obtained from all participants.

Discriminate criteria. Only OSAS patients were included in the study. Attention was paid to the fact that the study group did not have any other additional diseases like asthma, chronic obstructive pulmonary disease, pneumonia, psychiatric, diabetes, heart failure, and those who work at night work. Those with comorbidities were not included in the study.

Chemicals and reagents. The chemicals and reagents for agmatine analysis were purchased from the listed brands, respectively; agmatine sulfate sodium salt, o-phthalaldehyde (Sigma, USA), HPLC grade ultra-pure water (Tekkim, Turkey), HPLC grade acetonitrile and methanol (Carlo Erba, France), HPLC grade perchloric acid, 2-mercaptoethanol and acetic acid (Merck, Germany), fuming hydrochloric acid, potassium dihydrogen phosphate, potassium hydroxide and sodium hydroxide (Isolab, Germany), boric acid (Wisent Inc Canada), sodium octyl sulfate salt (Glentham Life Sciences, UK). The chemicals for trace element analysis were purchased from the mentioned respective brands; supra pure nitric acid (Carlo Erba, France), hydrogen peroxide (Merck, Germany), standard mix solution (Chem-Lab, 23 elements ICP-QC standard solutions, Belgium), internal standard germanium (Inorganic Ventures, USA). Ultrapure water (Millipore, Synerg UV, France) was used in all analyses.

Plasma/serum samples collection. In the morning, after the PSG and nocturnal fast of at least 8 hours, venous blood samples (5 ml) were collected in routine biochemistry blood tubes (Vacutte, USA) for serum separation and (5 ml) in lithium heparin tubes (Vacutte, USA) for plasma separation. Plasma/

serum samples were then centrifuged at 4000 rpm for 15 min. The plasma/serum samples obtained after centrifugation were portioned into microcentrifuge tubes, labeled, and stored at -80°C until the analysis was carried out.

Measurement of plasma trace element levels. Firstly, microwave digestion of plasma samples was performed. 1 ml plasma samples were added into teflon digestion tubes. 1 ml of 35% H_2O_2 and 2.5 ml of 67-69% supra pure HNO_3 were added to them, the caps were closed tightly and placed in the microwave digestion system (Cem Mars-6-One Touch Technology, USA). The device was operated according to the 'human blood analysis' method, which is ready in the system. After microwave digestion, the samples were taken into 50 ml falcon tubes and the final volume was made up to 25 ml by ultrapure water.

In order to prepare the calibration standards, 1 ppm standard was prepared from 100 ppm stock standard mix (include 23 different elements) solution of the elements to be analyzed. Then, by diluting from 1 ppm standard solution, new calibration standard solutions were prepared at 10 different concentrations (0.1-0.2-0.5-1-2-5-10-15-20-50 ppb). Calibration standard solutions were prepared in 2% HNO_3. A single internal standard germanium (Ge) was added at a concentration of 10 ppb to each of the prepared 10 different standard solutions.

The final step was determining the levels of the trace elements. After microwave digestion, a diluted 5 ml sample was taken and the internal standard (10 ppb) was added. Plasma Cu, Co, Mg, Mo, Zn, and Se levels were determined using ICP-MS (ThermoScientific, iCAP-Q, Germany). First, a calibration curve was plotted with the blank and calibration standard solutions readings. Prepared plasma samples were read 3 times, averaged, and expressed in ppb (µg/l) or ppm (mg/l).

Measurement of plasma agmatine levels. Plasma agmatine levels were determined by the method developed by Uzbay et al. (2013) [12]. Ultra high-pressure liquid chromatography (UHPLC) (Shimadzu Nexera X2, Japan) instrument was used. At first, samples were deproteinized, neutralized, derivatized, and cartridged, then injected into the UHPLC system. The standard curve was formed by plotting the peak area versus standard solution concentration graph of the agmatine standard peaks prepared at 3 different concentrations, the curve equation, and the R2 value was calculated. Plasma agmatine (ppm) levels were calculated by adding agmatine peak area values to the standard curve equation. Agmatine peaks were shown in Fig. 1 (*A*, *B*).

Measurement of serum telomerase levels. Serum telomerase (E.C.2.7.7.49) levels were determined using enzyme-linked immunosorbent assay (ELISA) kit (catalog number SG-11444, SinoGeneclon Co. Ltd, Hangzhou, China), based on a double sandwich system. The kit prospectus was followed at every stage of the assay. The range of the assay was 0.1 (ng/ml) - 4 (ng/ml), and the sensitivity was 0.03 (ng/ml).

Statistical analysis. The data were evaluated with Statistical Package for the Social Sciences (IBM SPSS Statistics, NY: IBM Corp) software, version 22. The sample size and study power were calculated using G*Power software, version 3.1. (Düsseldorf University, Germany). Using the data of another study, the effect size was determined as 0.90731 and the sample size was 90. Data were defined as mean, standard deviation (SD), and *P* values. According to the normality test (Kolmogorov Smirnov), it was decided to apply non-parametric tests, since the data are not normally distributed. Kruskal-Wallis (K-W) test was applied to the statistical significance of the difference in the parameters according to the groups. The Mann-Whitney U test was used to determine which group had a statistically significant difference between the variables. Statistical significance was accepted as ($P < 0.05$). The relationship and correlation coefficients between the variables were determined by Spearman's rho test.

Results

Demographic characteristics. There was no statistically significant difference between groups in terms of age and smoking habits ($P > 0.05$) but the difference in terms of gender was found significant ($P = 0.002$) (Table 1). Study groups were prevalently male (60 males, 66.6%; 30 females, 33.3%). In terms of mean BMI, a statistically significant difference was observed between mild-severe (31.3 ± 5.3 vs 34.3 ± 6.6 kg/m^2) and moderate-severe (30.7 ± 4.5 vs 34.3 ± 6.6 kg/m^2) patient groups ($P = 0.031$). BMI was highest in the severe patient groups (Fig. 2, *A*).

Clinical characteristics. Oxygen saturation percentages (SpO_2) showed a statistically significant difference among mild (90.4 ± 1.4%), moderate (89.4 ± 1.5%), and severe (85.7 ± 5.4%) patient groups ($P < 0.001$) (Fig. 2, *B*). SpO_2 percentages decreased inversely with disease severity.

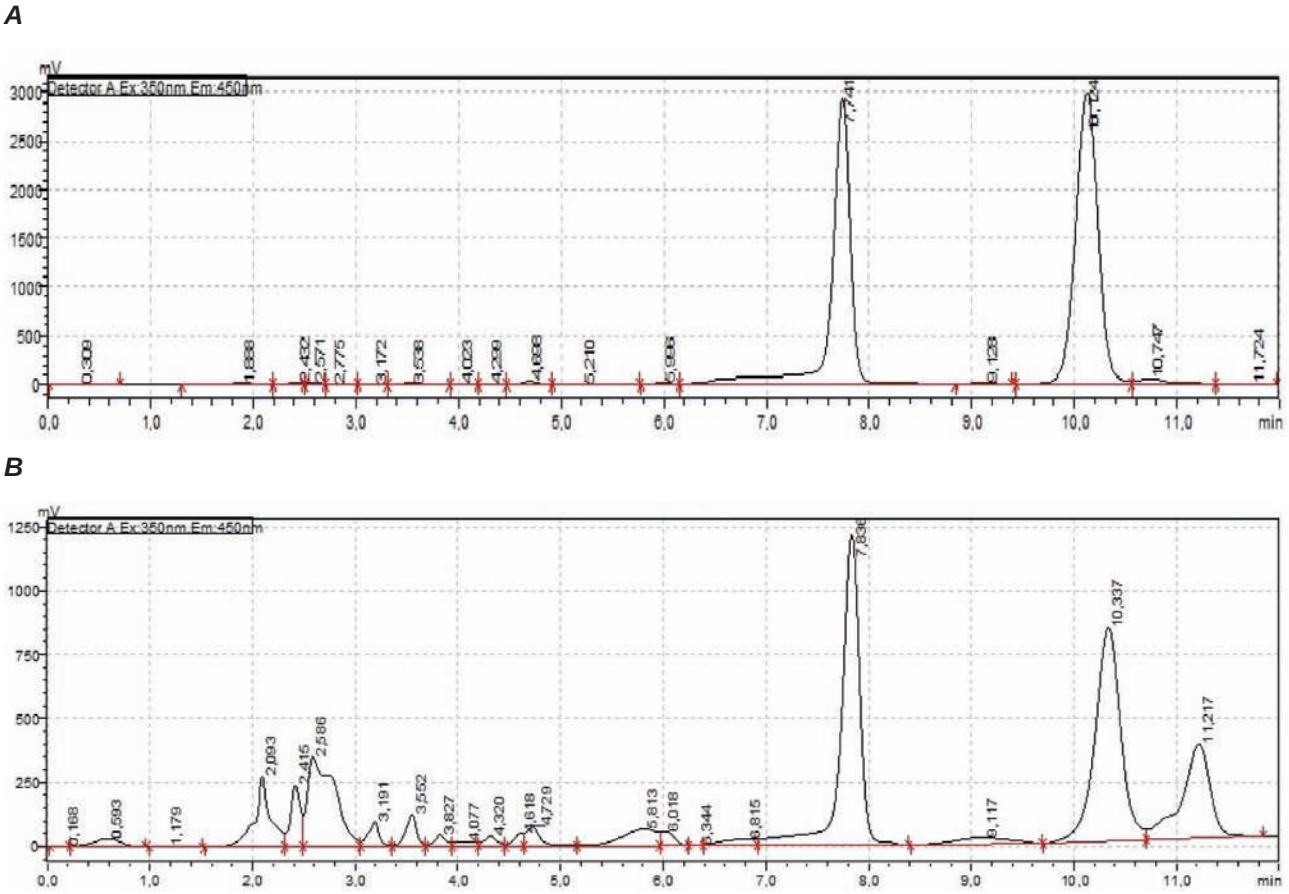

Fig. 1. Agmatine peaks. ***A*** *– The peak with a retention time of 7.741 min was the derivative reagent, and 10.124 min was the standard agmatine peak.* ***B*** *– The peak with a retention time of 7.838 min was the derivative reagent, and 10.337 min was the plasma agmatine peak*

Trace element levels. Plasma Co levels were significantly different between mild-severe (1.15 ± 0.71 µg/l, 2.11 ± 1.22 µg/l) and moderate-severe (1.27 ± 0.55 µg/l, 2.11 ± 1.22 µg/l) patient groups. Co levels were found to be the highest in the severe patient groups (P = 0.001) (Fig. 3). In addition to Co, plasma Se levels also were significantly different between mild-moderate (70.0 ± 26.3 µg/l, 99.8 ± 31.0 µg/l) and mild-severe (70.0 ± 26.0 µg/l, 88.8 ± 26.0 µg/l) patient groups. Se levels in the moderate patient group were found to be higher than in the severe and mild patient groups. Also, the Se levels in severe patient groups were higher than the mild patient groups (P < 0.001) (Fig. 4). There were no significant differences in other plasma trace element levels (Table 1).

Agmatine levels. Plasma agmatine levels were significantly different between mild-moderate (0.36 ± 0.17 ppm, 0.10 ± 0.08 ppm), mild-severe (0.36 ± 0.17 ppm, 0.05±0.03 ppm) and moderate-severe (0.10 ± 0.08 ppm, 0.05 ± 0.03 ppm) patient groups. Agmatine levels were highest in the mild patient group (P < 0.001) (Fig. 5).

Telomerase levels. Serum telomerase levels were significantly different between mild-moderate (0.87 ± 0.55 ng/ml, 0.56 ± 0.22 ng/ml), mild-severe (0.87 ± 0.55 ng/ml, 0.44 ± 0.09 ng/ml) and moderate-severe (0.56 ± 0.22 ng/ml, 0.44 ± 0.09 ng/ml) patient groups. Telomerase levels were highest in the mild patient group (P < 0.001) (Fig. 6).

Table 2 shows the correlation of plasma trace elements, agmatine, telomerase and other variables. AHI values showed statistically significant relationships with BMI, SpO_2, Co, Se, agmatine, and telomerase levels. AHI values were negatively correlated with SpO_2 (r = -0.58, P < 0.001), agmatine (r = -0.72, P < 0.001), telomerase (r = -0.47, P < 0.001) and positively correlated with BMI (r = 0.24, P =0.03), Co (r = 0.35, P = 0.001), Se (r = 0.41, P < 0.001). Also, BMI values were negatively correlated with SpO_2

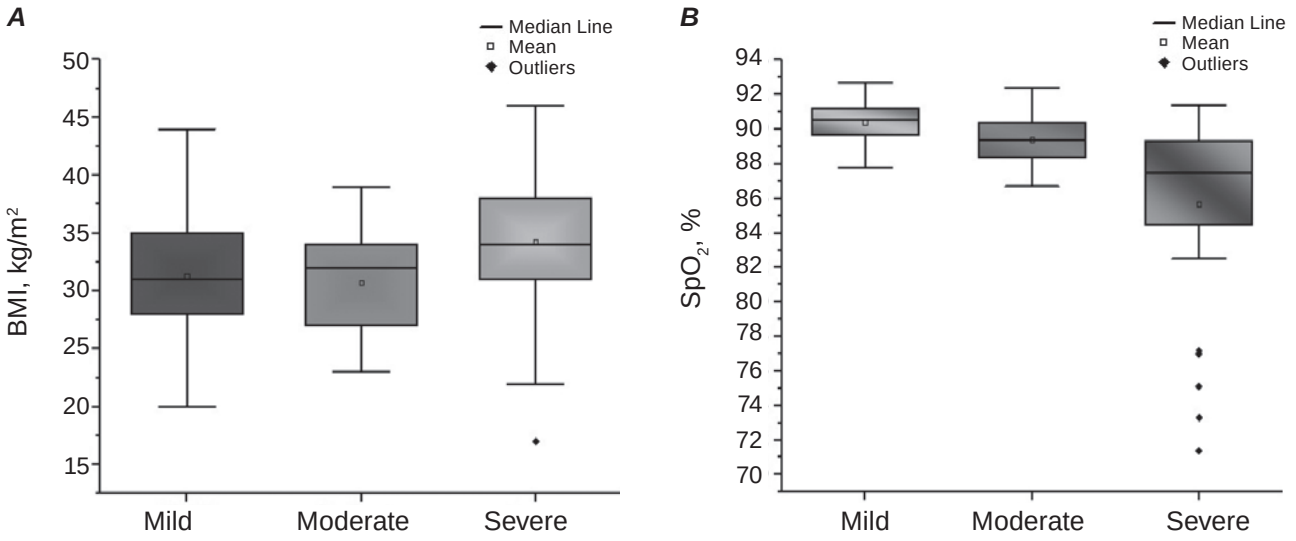

Fig. 2. ***A*** *– Body mass index, BMI (P = 0.031), and* ***B*** *– oxygen saturation, SpO_2 (P < 0.001)*

Table 1. Comparison of demographic and trace element variables of OSAS patients according to disease severity

Variable	Groups, (*n* = 30)			*P*
	Mild	Moderate	Severe	
Gender				
Female	12 (40%)	7 (23.3%)	11 (36.7%)	0.002*
Male	18 (60%)	23 (76.7%)	19 (63.3%)	0.002*
Smoking				
+	8 (26.7%)	13 (43.3%)	15 (50%)	0.058
–	22 (73.3%)	17 (56.7%)	15 (50%)	0.058
Age	46.00 ± 10.90	50.6 ± 10.7	52.00 ± 12.60	0.556
Cu, mg/l	1.08 ± 0.34	0.99 ± 0.22	1.09 ± 0.28	0.483
Mg, mg/l	25.70 ± 8.40	20.0 ± 3.14	21.30 ± 4.77	0.052
Mo, µg/l	5.10 ± 2.60	6.00 ± 2.60	7.20 ± 5.30	0.532
Zn, mg/l	0.94 ± 0.28	1.03 ± 0.36	0.94 ± 0.17	0.566

Data were expressed as mean ± SD where appropriate, *P < 0.05, group comparisons by Mann-Whitney U-test or Chi-Square test.

(r = -0.43, P < 0.001), and positively correlated with Cu (r = 0.3, P = 0.004). Agmatine were positively correlated with telomerase (r = 0.42, P < 0.001), SpO_2 (r = 0.38, P < 0.001) and Mg (r = 0.23, P = 0.03), negatively correlated with Co (r = -0.23, P = 0.03). Telomerase was positively correlated with SpO_2 (r = 0.26, P = 0.013). In addition, other trace elements showed various correlations among themselves.

Discussion

In this study, we evaluated the change in plasma trace element, agmatine, and serum telomerase levels in obstructive sleep apnea syndrome of different severity. The mild patient group is defined as the 'simple snoring group' and we considered them as the control group. In addition, we determined demographic data and variables such as SpO_2 and BMI to see how they changed with disease severity. BMI

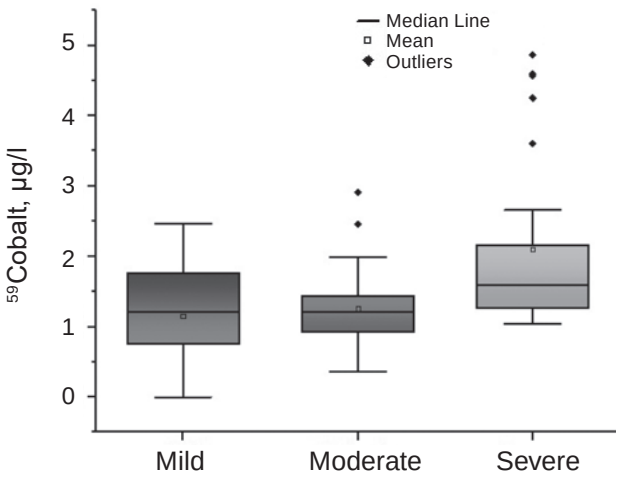

Fig. 3. Comparison of plasma cobalt (µg/l) levels (P = 0.001)

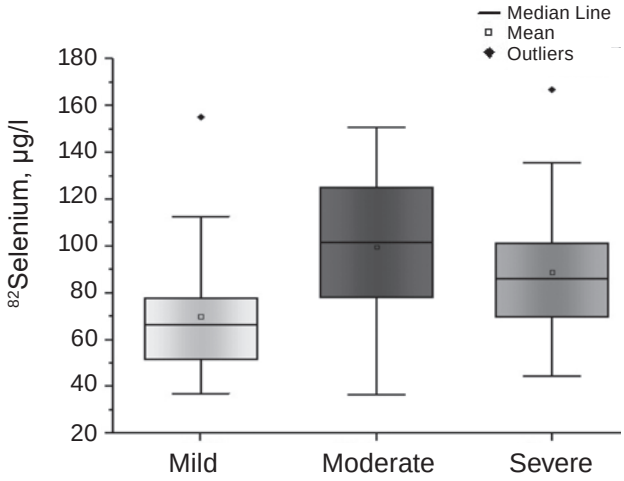

Fig. 4. Comparison of plasma selenium (µg/l) levels (P < 0.001)

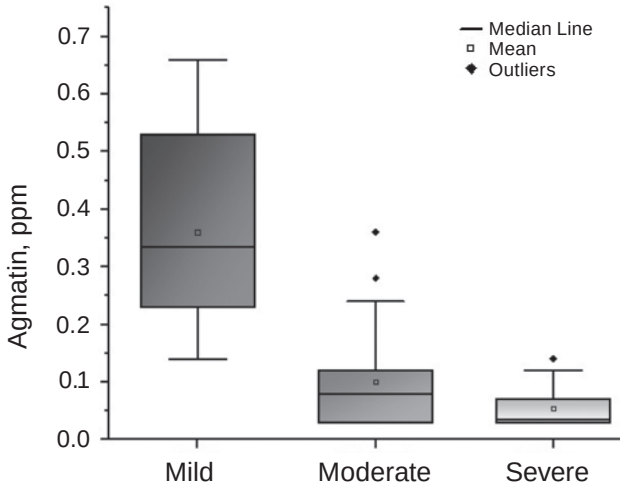

Fig. 5. Comparison of plasma agmatine (ppm) levels (P < 0.001)

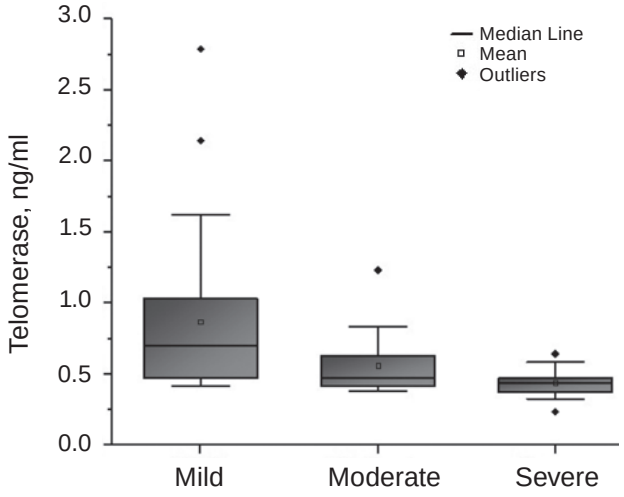

Fig. 6. Comparison of serum telomerase (ng/ml) levels (P < 0.000)

values were associated with OSAS severity which was indicated by AHI values. We found BMI values higher in severe OSAS compared to mild and moderate OSAS patients.

The presence of sleep-related hypoxia is known in OSAS, because of this, they had significantly lower oxygen saturation [1]. SpO_2 values were found to be lower in severe OSAS compared to other groups and showed a negative correlation with disease severity, BMI, Co, and Se levels relation. In the present study, SpO_2 values indicated that severe patients were exposed to intermittent hypoxia.

Hypoxic conditions lead to a lack of a main electron acceptor in the respiratory chain, resulting in a reduction of adenosine triphosphate (ATP). This reduction has negative effects on vital functions, including many enzymatic pathways activated by trace elements. Many trace elements also play an important role in enzymatic reactions and oxidant/antioxidant balance. For this reason, trace elements may be indirectly or directly involved in the pathophysiology of some diseases [13]. Information about trace element levels in OSAS and their contribution to the pathophysiology of the disease has not yet

Table 2. Correlation of demographic and biochemical variables

Variable	Correlate	*r*	*P* value
AHI	BMI	0.24	0.025*
	SpO_2	-0.58	<0.001*
	Co	0.35	0.001*
	Se	0.41	<0.001*
	Agmatin	-0.72	<0.001*
	Telomerase	-0.47	<0.001*
BMI	SpO_2	-0.43	<0.001*
	Cu	0.30	0.004*
Co	SpO_2	-0.30	0.004*
Se	Cu	0.39	<0.001*
	Zn	0.40	<0.001*
	Mo	0.32	0.002*
	SpO_2	-0.30	0.004*
Cu	Zn	0.48	<0.001*
	Mo	0.33	0.001*
	Mg	0.51	<0.001*
Zn	Mo	0.26	0.013*
	Mg	0.32	0.002*
Agmatin	Telomerase	0.42	<0.001*
	Co	-0.23	0.029*
	Mg	0.23	0.032*
	SpO_2	0.38	<0.001*
Telomerase	SpO_2	0.26	0.013*

AHI (apnea-hypopnea index), BMI (Body mass index), SpO_2 (%) (oxygen saturation percentage). *Spearman's rho correlations.

been clarified. In this current study, while there was a significant difference in terms of Co and Se levels compared to the severity of the disease, no significant difference was found in terms of Cu, Mg, Mo, and Zn levels.

Selenium is an important trace element in the human body and plays a significant role in the protection of cell membranes from oxidative damage. Se deficiency reduces antioxidant activity and has been reported to interfere with the scavenging of free radicals, especially in systemic inflammatory diseases [14]. Chen et al. compared the Se levels of the control group and moderate OSAS patients and found the Se concentrations to be significantly reduced and assumed that this result reflects oxidative damage [15]. Contrary to this study, Saruhan et al. found increased Se levels in severe OSAS patients compared to the control group [16]. Studies reporting the role of Se on the pathogenesis of OSAS in the literature are limited to only these two studies. In this study, we obtained results consistent with the study of Saruhan et al. Se levels were found to be significantly higher in the moderate and severe patient groups compared to the mild patient group. The importance of increased Se in our patients is unknown. Se reduces inflammatory responses and is essential for immune system function in disease conditions [17]. Accordingly, Se levels may be increased to have a protective effect against inflammatory factors and reactive oxygen species, which are known to be elevated in OSAS patients [1, 18]. Another point of view is that Se levels might be increased with disease severity because selenoproteins developed an adaptation mechanism against chronic hypoxia and oxidative stress [16].

Cobalt is an essential trace element that is integrated into vitamin B_{12} (cobalamin), which is of great importance for folate and fatty acid metabolism, and it is found in almost all of the vitamin B_{12} found in healthy mammalian tissues. Gastrointestinal absorption of Co salts varies with the type of compound ingested dose, and the presence of other substances. Co is extensively bound to serum albumin, with 5-12% of the total Co in the body [19]. In the present study, plasma Co levels were found to be significantly higher in the severe patient group when compared to other patient groups. The reason for high Co levels in severe OSAS can be considered as increased absorption or decreased excretion of Co. Nevertheless, this issue needs more explanation.

In our study, it was found that plasma trace element levels were correlated with each other and there were complex interactions between these substances. Therefore, alterations in the concentration of one element can affect other elements and this leads to pathological events.

According to our knowledge, this is a unique study to measure plasma levels of agmatine in OSAS. Studies on agmatine are generally focused on its contribution to the treatment and pathophysiology of diseases with exogenous agmatine supplementation. There is a limited number of studies measuring agmatine levels and their results vary. Agmatine levels were found to be significantly higher in neuropsychological diseases such as schizophrenia [12],

attention deficit and hyperactivity disorder [20], compared to the control group. Unlike these studies, plasma levels of agmatine in patients with metabolic syndrome were found reduced compared with their controls [21].

Some of the important consequences of OSAS accompanied by intermittent hypoxia are cognitive dysfunction, cardiovascular pathologies, and ischemic strokes [22]. We hypothesized that there might be an association between agmatine and OSAS severity with certain aspects of hypoxia, cognitive impairment, and ischemic stroke biology. There is no information about both the physiological and pathological mechanism of agmatine and its contribution to the pathophysiology of OSAS. The antagonistic effect on glutamatergic N-Methyl-D-aspartate (NMDA) receptors and agonist effect on α2-adrenergic and imidazoline receptors are one of the best-known effects of agmatine [23]. Recurrent apneas cause very high levels of glutamate production, which leads to apoptosis with toxic effects on hippocampal neurons [24]. A cell culture study reported that agmatine has protective effects against cell damage caused by NMDA and glutamate excitotoxicity [23]. In light of this information, it can be suggested that agmatine contributes to glutamatergic dysfunction in OSAS. Another well-known effect of agmatine is on inhibition of NOS [8]. Again in a cell culture study, agmatine decreased hypoxic damage by inhibiting nitric oxide (NO) production [25]. Endothelial dysfunction leads to changes in cerebral and myocardial perfusion. In all of these, it may be one of the most likely causes of ischemic stroke and neurobehavioral deficiencies in OSAS by causing brain infarction development [22]. We thought that the increased hypoxia and endothelial dysfunction in OSAS may have caused a decrease in both NO and agmatine levels at the substrate level, by reducing their substrate L-arginine levels [26]. Decreased L-arginine levels in OSAS also support our opinion [27]. Because of these properties of agmatine, we hypothesized that OSAS might be affected by agmatine levels. As we expected in the present study, plasma agmatine levels of OSAS patients decreased as the disease severity increased.

Our study, which is related to the decrease in plasma agmatine levels with disease severity, showed that agmatine may be a target molecule for the pathophysiology of OSAS. Additional studies needed by adding a control group and including more subjects will further elucidate the contribution of agmatine to the pathophysiology of OSAS. Moreover, it is thought that it may be useful to investigate the therapeutic effect of agmatine on OSAS, in addition to the case studies in which many disorders are eliminated with agmatine treatment. Agmatine concentrations must be evaluated in other sleep and breathing disorders.

Telomeres are repeats of complex DNA sequences found at the end of eukaryotic chromosomes and dynamic regulators of cellular lifespan and chromosome integrity. Due to insufficient replication, telomere length gradually shortens with each division. Therefore, telomere length is considered a marker of cellular aging. Telomere shortening is mainly compensated by the enzyme telomerase, which adds back the telomeric DNA [28]. Hypoxia is the primary trigger of OSAS, and a study in a cell culture model exposed to various levels of hypoxia looked at the length of telomeres and telomerase activity. In a different study, telomerase activity in the blood of OSAS patients with high AHI was found to be lower and statistically significant compared to the control group [29]. Investigator Boyer et al. reported the association of recurrent hypoxemia and desaturation with shortened telomeres in OSAS patients [10].

In this current study, a statistically significant difference was found between the three groups in serum telomerase levels. The highest telomerase level was found in the mild patient group, while the telomerase levels of the moderate patient group were higher than the severe patients. We obtained results that were consistent with our literature review. As the severity of the disease increased, both a decrease in SpO_2 percentages and, a decrease in telomerase levels were observed. Reduced telomerase levels and shortened telomere lengths are associated with hypoxia and OS [30].

If the limitations of this study were listed, firstly it would be more clear if the patients were compared with the control group. Although we consider the mild patient group as the control group and compare accordingly, it would be more efficient to have a control group. Knowing whether the study groups received dietary supplements could also be useful in the evaluation of trace element levels. An alternative explanation for high trace element levels might be the exposure to potential environmental, food, and water pollution or contamination during blood collection and experimental stages. In this sense, it is very difficult to know the exposure of patients due to the ecosystem and contamination, which limits our study.

Conclusion. As a result, it was found that with the increase in the severity of OSAS disease, some plasma trace element levels increased, agmatine and telomerase levels reduced. The severity of the disease was also associated with BMI, and SpO_2. Furthermore, our current study gained specificity by analyzing numerous trace elements in the plasma of OSAS patients, at the same time with a very sensitive technique such as ICP-MS and comparing them according to the severity of the disease. Also, the first study was to measure agmatine levels in OSAS and compare disease severity. More studies are needed on agmatine in OSAS patients.

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Conflct of interest. Authors have completed the Unified Conflicts of Interest form at http://ukrbiochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

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РІВНІ АГМАТИНУ, ТЕЛОМЕРАЗИ ТА МІКРОЕЛЕМЕНТІВ У ПАЦІЄНТІВ ІЗ СИНДРОМОМ ОБСТРУКТИВНОГО АПНОЕ СНУ

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Синдром обструктивного апное сну (СОАС) характеризується рецидивуючими, частковими або повними обтураціями верхніх дихальних шляхів, що призводять до гіпоксії та біоелектричних реакцій неспання у поєднанні зі сном. Дані щодо біохімічних шляхів, які можуть обумовлювати негативні ефекти у хворих на СОАС із різним ступенем тяжкості захворювання, є обмеженими та різнорідними. Метою нашої роботи було оцінити рівні поліаміну агматину, який діє на центральну нервову систему, теломерази та мікроелементів у плазмі крові хворих на СОАС. У дослідженні брали участь 90 пацієнтів-добровольців із діагнозом СОАС, яких було розподілено на три групи по 30 осіб за показником індексу апное-гіпопное (ІАГ): легкий, помірний та тяжкий ступінь тяжкості. Вимірювали нічний відсоток насичення крові киснем (SpO_2) та індекс маси тіла (ІМТ). Рівень агматину в плазмі крові визначали методом ультра високоефективної рідинної хроматографії (UHPLC), рівень мікроелементів (Cu, Co, Mg, Mo, Zn, Se) у плазмі крові визначали методом мас-спектрометрії з індуктивно-зв'язаною плазмою (ICP-MS), рівень теломерази у сироватці крові – методом імуноензимного аналізу (ELISA). Виявлено, що рівень SpO_2 знижувався по мірі прогресування захворювання і мав негативну кореляцію з ІМТ, рівнями Co і Se в плазмі крові. Показано, що рівні агматину та теломерази були нижчими у пацієнтів із тяжким перебігом СОАС порівняно з іншими групами.

К л ю ч о в і с л о в а: синдром апное сну, агматин, теломераза, мікроелемент, SpO_2.

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