Wydawnictwo UR 2022
ISSN 2544-1361 (online)
doi: 10.15584/ejcem.2022.4.7

http://www.ejcem.ur.edu.pl
European Journal of Clinical and Experimental Medicine
Eur J Clin Exp Med 2022; 20 (4): 423–429

ORIGINAL PAPER

Zinc in fibromyalgia patients: relationship with body mass index and sleep quality

Ece Yiğit

Department of Internal Medicine, Faculty of Medicine, Istanbul Medipol University, İstanbul, Turkey

ABSTRACT

Introduction and aim. Given the potential relationship between oxidative stress and fibromyalgia and well-documented antioxidant efficacy of zinc, the present study aimed to determine serum zinc concentration in FM patients as compared to healthy controls, as well as to identify the correlation of serum zinc concentration with the body mass index (BMI) and sleep quality,

Material and methods. In this case-control study, 54 fibromyalgia patients were consecutively recruited between October 01, 2021 and December 01, 2021. The control group consisted of 54 age- and sex-matched healthy controls.

Results. Fibromyalgia group had significantly lower zinc concentration, higher body mass index, and lower sleep quality scores as compared to the healthy control group. The correlation analysis revealed a significantly negative correlation between serum zinc concentration and body mass index and a significantly positive correlation between serum zinc concentration and sleep quality both in fibromyalgia and healthy control groups.

Conclusion. Our results both support the hypothesis that low serum zinc concentration plays a role in the pathophysiology of fibromyalgia and indicate that fibromyalgia may lead to weight gain and poor sleep quality, which needs to be confirmed in large-cohort studies.

Keywords. body mass index, fibromyalgia, sleep quality, zinc

Introduction

Fibromyalgia (FM) is a disease characterized by widespread musculoskeletal pain of unknown etiology.[1,2] Its prevalence is reported between 2% and 5% depending on age, sex and specific populations, with women being 2-3 times more likely to have this disease as compared with men.[2,3] In our country, the prevalence of FM ranges from 3.6% in adult females to 31% in geriatric population.[4-6]

The diagnosis of FM is usually established using the American College of Rheumatology (ACR) criteria, which requires presence of pain in at least 11 of the 18 tender points throughout the body on palpation for at least 3 months, with the combination of patient history, physical examination and laboratory analysis contributing to the diagnosis.[7,8]

In addition to widespread pain, patients with FM also present with accompanying conditions such as sleep disorder, mood disorder, cognitive disorder, headache, restless leg and fatigue. Pain, fatigue, and sleep disorder are the most common conditions that every patient with FM presents with.[1,7]

Although the etiology and pathogenesis of FM is yet to be clarified, interaction between genetic, immunologic, neuroendocrine, environmental, psychological and nutritional factors is thought to be involved in its pathogenesis.[1,8] The role of oxidative stress in the pathogenesis of FM is well documented. Low serum levels of antioxidant elements, particularly those involved in the redox process such as magnesium, zinc, and selenium, have been demonstrated in some FM

Corresponding author: Ece Yigit, e-mail: eceyigit@medipol.edu.tr

Received: 24.08.2022 / Revised: 12.10.2022 / Accepted: 20.10.2022 / Published: 30.12.2022

Yiğit E. *Zinc in fibromyalgia patients: relationship with body mass index and sleep quality.* Eur J Clin Exp Med. 2022;20(4):423–429. doi: 10.15584/ejcem.2022.4.7.

patients. Moreover, serum magnesium and zinc levels are also associated with clinical parameters in FM, indicating their potential role in the pathogenesis of the disease.[9-12]

Zinc is an essential element required for various systems to function properly. It naturally exists in some foods and is also available as a dietary supplement. Recommended daily amount of zinc is 11 mg for adult males and 8 mg for adult females.[13] It is involved in the catalytic activity of nearly 100 enzymes as a cofactor and plays a role in numerous cellular metabolisms with its well-documented antioxidant role.[11,14]

Aim

Given the potential relationship between oxidative stress and FM and well-documented antioxidant efficacy of zinc, the present study aimed to determine serum zinc concentration in FM patients as compared to healthy controls, as well as to identify the correlation of serum zinc concentration with the body mass index (BMI) and sleep quality, both of which are frequently encountered in patients with FM.

Material and methods

This single-center case-control prospective study was carried out between October 01, 2021 and December 01, 2021 in the Istanbul Medipol University School of Medicine, Department of Internal Medicine, Istanbul Turkey. The study was approved by the Non-Interventional Clinical Research Ethics Committee of Istanbul Medipol University (Date 14/10/2021, Decision No:1009).

The study population consisted of 108 subjects aged ≥18 years [consecutively recruited 54 FM patients who met the ACR 2016 criteria and were otherwise healthy, and 54 age- and sex-matched healthy controls (HCs)].[15]

All subjects were informed about the purpose and design of the study in detail, and those who agreed to participate in the study and signed the informed voluntary consent form were enrolled.

A detailed medical history was obtained from all participants, and their physical examination including measurement of height and body weight was performed. The height was measured using a stadiometer with accuracy of 0.1 cm, and the body height was measured using a Tanita scale with accuracy of 0.1kg (Tanita Body Composition Analyzer, MC-780MA-N, Japan). The BMI was calculated as the body weight in kilograms divided by the square of the height in meters (kg/m^2). The patients in each group were then classified according to their BMI defined by the World Health Organization as normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2) and obese (≥30 kg/m^2).[16] Study exclusion criteria for all subjects were the history of chronic diseases, drug use, alcohol consumption, smoking and drug abuse, pathological findings on physical examination, and laboratory analyses indicating presence of a comorbid condition.

Blood samples for complete blood count, routine biochemical analyses [alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea, creatinine, thyroid-stimulating hormone (TSH), fasting blood glucose, total cholesterol, low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, triglyceride], and measurement of serum zinc concentration were collected from all study participants in the morning after 12-hour fasting period.

Serum zinc concentration was measured using the Randox colorimetric assay for zinc (United Kingdom) and then compared between the FM and HC groups. For the measurement of serum zinc concentration, 6 mL blood sample was taken into the heavy metal-free trace element tubes containing heparin. The blood was centrifuged at 2500 rpm for 10 minutes. Zinc concentrations were expressed in μg/dL.

Sleep quality in both groups was assessed using the Richards Campbell Sleep Questionnaire (RCSQ), which showed excellent internal consistency and moderate correlation with polysomnographic recording -the gold standard in measuring sleep quality. The RCSQ is a five-item self-administered questionnaire used to assess perceived sleep depth, sleep latency, efficiency of sleep, sleep quality and the number of awakenings during sleep. Subsequently, a 6th item -night-time noise- was included in the RCSQ. Each of the sleep parameters is rated from 0 (the worst possible sleep) to 100 (the best sleep) on a visual analogue scale. The total score ranges between 0 and 600, which is then divided by six to obtain a mean total score for each patient (0-25: very poor sleep quality, 75-100 good sleep quality).[17,18] The validity and reliability study of the Turkish version of RCSQ was performed in 2015 by Ozlu and Ozer.[19]

Statistical analysis

Data was analyzed using the MedCalc® Statistical Software Program version 19.7.2 (MedCalc Software Ltd, Ostend, Belgium). Descriptive statistics (mean, standard deviation, median, minimum and maximum) were presented for continuous variables. The normality of continuous variables was analyzed by Shapiro-Wilks test. Two independent normally distributed variables were compared using the Student t-test, whereas Mann-Whitney U test was used for the comparison of two independent non-normally distributed variables. The relationship between categorical variables was analyzed using the Chi-square test, in combination with Yates Continuity Correction Chi-Square, where available. The relationship between two variables was determined using the Pearson's correlation coefficient for normally distributed variables and using the Spearman's rho correlation for non-normally distributed variables.

The level of statistical significance was set at p <0.05. Univariate and multivariate logistic regression analyses including serum zinc, RCSQ sleep score and BMI were performed.

Results

A total of 108 subjects (54 in each of the FM and HC groups) were included in the study. Overall, 91 (84.3%) of the study population were female and 17 (15.7%) were male. There was no difference between the FM and HC groups in terms of gender distribution (FM group: 46 [85.2%] females and 8 [14.8%] males; HC group: 45 [83.3%] females and 9 [16.7%] males; p=1.00). The mean age of the study population was 42±10.3 years (range, 24-63 years). The FM and HC groups were comparable in terms of the mean age of the participants (42.6±9.8 years [range, 25-61 years] and 41.4±10.9 years [range, 24-63 years], respectively; p=0.559). The mean serum zinc concentration of the study population was 79.6±17.1 ug/dL (range, 42-128 μg/dL), with significantly lower concentrations detected in the FM group vs. the HC group (73.6±15.1 μg/dL [range, 42-102 μg/dL] vs. 85.7±17 ug/dL [range, 49-128 μg/dL]; p≤0.001). The mean BMI of the whole study group was 26.1±4.5 kg/m^2 (range, 18.2-37.5 kg/m^2). The FM group had significantly higher BMI compared to the HC group (FM group: 27.3±4.6 kg/m^2 [18.2-37.5 kg/m^2] and HC group: 24.8±4.2 kg/m^2 [18.2-32.8 kg/m^2]; p=0.003). With regard to the mean sleep quality score, it was 63.0±12.7 in the whole study population, and it was significantly lower in the FM group than the HC group [58.1±11.3 vs. 67.8±12.3; p≤0.001], indicating poorer sleep quality in the FM group. The general characteristics of the whole study population and according to FM and healthy control groups are demonstrated in Table 1.

Table 1. General characteristics of the whole study population and according to study groups[a]

Characteristics	Study population	FM Group	HC Group	p
	n=108	n=54	n=54	
Sex				
Female, n (%)	91	46 (85.2)	45 (83.3)	1.00*
Male, n (%)	17	8 (14.8)	9 (16.7)	
Age, years, mean±SD	42±10.3	42.6±9.8	41.4±10.9	0.559**
Zinc, ug/dL, mean±SD	79.6±17.1	73.6±15.1	85.7±17	<0.001**
RCSQ Score, mean±SD	63.0±12.7	58.1±11.3	67.8±12.3	<0.001***
BMI, kg/m^2, mean±SD	26.1±4.5	27.3±4.6	24.8±4.2	0.003***

[a] *Yates continuity correction, **Student's t-test, ***Mann-Whitney U test; FM – fibromyalgia; HC – healthy control; SD – standard deviation; BMI – body mass index; RCSQ – Richards Campbell Sleep Questionnaire

The correlation analysis between serum zinc concentration and BMI revealed a significantly negative correlation in the whole study population (r=-0.719, p<0.001) and in the FM and HC groups (r=-0.726, p<0.001 and r=-0.648, p<0.001, respectively).

The correlation of serum zinc concentration with sleep quality and BMI is demonstrated in Table 2.

Table 2. Correlation of serum zinc concentration with sleep scores and body mass index in the whole study population and according to study groups[a]

	Sleep score		BMI	
Serum Zinc	r	p	r	p
Study population	0.824**	<0.001	-0.719*	<0.001
FM Group	0.751*	<0.001	-0.726*	<0.001
HC Group	0.861**	<0.001	-0.648**	<0.001

[a] *Pearson's correlation coefficient, **Spearman's correlation coefficient; FM – fibromyalgia; HC – healthy control; BMI – body mass index

Regarding the correlation between serum zinc concentration and sleep quality, a significantly strong correlation was detected both in the overall study population and in the HC group (r=0.824, p<0.001 and r=0.861, p<0.001, respectively), and a good correlation was detected in the FM group (r=0.751, p<0.001). Univariate and multivariate regression analyzes are shown in Table 3.

Table 3. Univariate and multivariate regression analyzes

	Univariate Logistic Regression			Multivariate Logistic Regression		
	Sig	OR	95 % CI	Sig	OR	95 % CI
Zinc	<0.001	0.954	0.93–0.98	0.438		
Sleep Score	<0.001	0.989	0.98–0.99	<0.001	0.989	0.98–0.99
BMI	0.005	1.141	0.04–1.25	0.944		

Univariate regression analysis revealed that fibromyalgia was associated with both zinc and RCSQ sleep score and BMI. However, when the multivariate logistic regression analysis was examined, it was seen that this relationship was only between fibromyalgia and RSCQ sleep score.

Discussion

The present study, which investigated serum zinc concentrations in FM patients compared to the controls and its relationship with sleep quality and BMI, found significantly lower zinc concentration in the FM group and showed significant correlation with sleep quality and BMI.

Fibromyalgia is a painful condition affecting every population across the world. FM presents itself not only with pain, but also with various clinical conditions including mood disorders (such as anxiety, depression),

sleep disorders, restless leg syndrome, and chronic fatigue syndrome (CFS), each of which impairs the patient quality of life.[1] Thereby, prevention and treatment of this disorder is of great importance for patient quality of life. However, being aware of the pathogenesis of the disease is essential to establish accurate preventive measures.

Although the pathophysiology of FM is yet unclear, several mechanisms have been proposed, including the oxidative stress. Altindag and Celik reported significantly lower total plasma antioxidant capacity in FM patients than in healthy controls, supporting the role of antioxidants in the pathogenesis of FM.[20] Given that some trace elements, such as magnesium, zinc, and selenium are essential for some antioxidant enzymes and that oxidative stress is one of the mechanisms in the pathophysiology of FM, it has been suggested that deficiency of these elements might be involved in the pathophysiology of FM and related clinical conditions.[2,9-11,21-24]

Zinc is the second most important element for life following iron, and it is found in all tissues, fluids and secretions with total amount to be approximately 2–4 g.[13] Along with well-documented antioxidant efficacy of zinc, the role of serum zinc concentration in the etiology of FM and its relationship with clinical conditions has recently become the subject of interest.[11]

In a manner supporting the hypothesis that zinc plays a role in the pathophysiology of FM due to its antioxidant effect, a study reported lower zinc concentrations and higher levels of oxidative stress markers in the FM patients compared to the healthy controls. In that study, zinc showed strong negative correlation with the number of tender points, where magnesium showed moderate negative correlation. Moreover, oxidative stress markers also showed negative correlation with zinc and magnesium.[25]

In our country, significantly lower serum zinc and magnesium concentrations were determined in FM patients compared to the healthy controls, whereas no significant difference was found for serum selenium concentration. A significant correlation was demonstrated between zinc concentration and the number of tender points, suggesting that these elements might play a role in the pathogenesis of FM.[9,12,26] However, in the present study, we did not investigate the oxidative status of the FM patients or the association between zinc concentration and tender points, which may be considered a limitation for the present study.

Serum zinc concentration is low also in the patients with CFS and myofascial pain syndrome.[27,28] In addition, the erythrocyte concentration of zinc was found to be associated with pain in the patients with myofascial pain syndrome.[12] All of these findings support the impact of low zinc concentration on pain in FM patients.

A prospective study conducted in 60 Iraqi FM patients diagnosed based on the ACR criteria found significantly lower serum magnesium, calcium, and zinc concentrations in the patients with FM than healthy controls. They concluded that levels of these elements may be a good indicator to evaluate this disease.[14]

Contrary to the studies demonstrating low serum zinc concentrations in FM patients than in the controls,[9,12,14,24] Rosborg et al., who compared the concentrations of 30 elements in the whole blood, urine, and drinking water in female patients with FM and matching controls, found higher serum zinc concentrations in FM patients.[21] The results of this study did not support the hypothesis that trace elements including zinc play a role in the development of FM.[23] Likewise, a systematic review and meta-analysis of 5 randomized controlled trials and 40 observational studies investigating mineral and vitamin deficiencies in the patients with FM and with CFS failed to find sufficient evidence to support the hypothesis that vitamin and mineral deficiencies play a role in the pathophysiology of CFS or FM syndrome.[29]

These contradictory results reported in the studies investigating the role of trace elements in the pathogenesis of FM might be due to the differences between the studies in terms of sample size, study methods, specimens (such as whole blood, serum, and erythrocyte) used for the measurement of zinc concentration or the criteria used for the diagnosis of FM. In addition, time of blood sample collection for zinc measurement is also important since zinc concentration is affected by many factors.

In the present study, we demonstrated significantly lower serum zinc concentration in the FM group and supported that zinc was involved in the pathogenesis of FM, as was confirmed in many studies.

Obesity is also one of the clinical conditions that are frequently encountered in FM patients. Although the relationship between obesity and chronic musculoskeletal pain remains unclear, the prevalence of obesity in people with chronic musculoskeletal pain is high as 37-65%.[30] Such a high prevalence of obesity in the patients with chronic musculoskeletal pain including FM may result from the oxidative stress playing a role in the pathophysiology of obesity and FM or may be due to the pain itself, which restricts the activities of daily living and results in weight gain.[31] This was confirmed also in the present study, where the mean BMI value of the FM group was significantly higher than that of the HC group, even though BMI values in the FM group indicated rather overweight than obesity.

Zinc not only plays an important role in many biochemical and metabolic processes as a cofactor of some enzymes including those involving in the pathophysiology of obesity, but also participates in carbohydrate,

protein, and lipid metabolisms indicating its potential role in the pathophysiology of obesity.[32] The relationship between zinc and obesity, particularly in the presence of inflammation and oxidative stress, has been demonstrated in earlier studies.[32,33] Serum zinc concentration was found low in obese people, showing a negative correlation with BMI, particularly when compared with those with normal weight.[34] Moreover, a negative correlation was demonstrated also between low serum zinc concentration and insulin resistance in perimenopausal obese women.[35] In a study, no relationship was demonstrated between serum zinc concentration and BMI; however, an inverse relationship was determined between erythrocyte zinc concentration and BMI, suggesting that erythrocyte concentration of zinc might be a more reliable parameter in assessing zinc status.[36] Despite normal serum zinc concentrations both in the obese group and in the control group, a study reported lower serum zinc concentration in the obese group, which did not reach the level of statistical significance. However, a significantly negative correlation was demonstrated between serum zinc concentration and BMI.[37] In the present study, similarly, serum zinc concentration was within the normal range in both groups regardless of the BMI value. The correlation analysis revealed significantly negative correlation between zinc concentration and BMI in the whole study population and in both groups regardless of the pain status. The results indicating a negative correlation between zinc concentrations and BMI values suggest that FM patients have higher BMI values because of, at least in part, low serum zinc concentrations as well as limited activity due to pain.

The interaction between obesity, pain, and poor sleep quality is well-documented.[38,39] Sleep is essential for our body and mind to rest at night and to wake up in the morning as refreshed; thus, poor sleep or sleep quality has a considerable impact on daily life as well as well-being. FM is usually accompanied by sleep disorders due not only to obesity but also to the widespread pain, causing the people to hardly perform and maintain the activities of daily living. Considering that zinc plays a role in the pathophysiology of both obesity and FM, we hypothesized that it might be playing a role also in sleep quality in FM patients.

Although a Chinese cohort study failed to demonstrate any effect of blood zinc concentration on sleep quality at preschool age, lower blood zinc concentration in preschool age was predictive of poor sleep quality at adolescence and higher blood zinc concentration was associated with better sleep quality, underlining potential importance of zinc concentrations in early childhood.[40] In contrast, a study found no significant difference between the hemodialysis patients with and without sleep disturbances in terms of blood zinc, manganese, copper, and lead levels, but low blood selenium levels were associated with severe sleep disturbance.[41]

In addition to the limited number of studies investigating the effects of zinc concentrations in various body fluids on sleep quality, several studies also investigated the effect of zinc consumption or zinc supplements on sleep quality. A study investigating sleep quality in female students based on zinc consumption found no difference in sleep quality of those consuming adequate vs. inadequate amount of zinc. However, zinc intake showed a significant association with sleep delay and mental quality of sleep.[42] Effect of melatonin plus zinc supplement (M+Z) on sleep parameters in the patients with CFS was investigated in a randomized, double-blind, placebo-controlled study. In that study, sleep quality and sleep latency improved with treatment in both M+Z and placebo groups; however, sleep latency worsened after treatment discontinuation in the M+Z group. No difference was determined between the groups in any parameters of Pittsburgh Sleep Quality Index.[43] Conflicting results reported in the studies might have arisen from different scales used to assess sleep parameters.

The results of our study showed that there is a direct relationship between fibromyalgia and sleep quality. This is understandable given that fibromyalgia patients have lower zinc levels and a higher BMI and both of these factors affect sleep quality. Detection of lower zinc levels, worse sleep quality and higher BMI in fibromyalgia patients compared to the control group is due to the close relationship between these 3 conditions.

Our study has some limitations. First, low sample size and cross-sectional design of the study make it difficult to draw a definite conclusion. Besides, the major limitation was the fact that zinc concentration was studied only in the serum. Erythrocyte concentration of zinc may give more accurate results, because the majority of zinc in the body is found intracellularly.

Conclusion

Our results do not only support the hypothesis that low serum zinc concentration plays a role in the pathophysiology of FM but also indicate that FM may lead to weight gain and poor sleep quality, which needs to be confirmed in large-cohort studies. Studies investigating zinc concentrations in other tissue samples including erythrocytes (intracellular concentration) and showing an improvement in pain and related clinical conditions after treatment with zinc supplements are required to draw further and more precise conclusion.

Declarations

Funding

The authors declared that this study has received no financial support or any funding.

Author contributions

Conceptualization, E.Y.; Methodology, E.Y.; Formal Analysis, E.Y.; Investigation, E.Y.; Resources, E.Y.; Writing – Original Draft Preparation, E.Y.; Writing – Review & Editing, E.Y.; Visualization, E.Y.; Supervision, E.Y.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

The study was approved by the Non-Interventional Clinical Research Ethics Committee of Istanbul Medipol University (Date 14/10/2021, Decision No:1009).

References

1. Clauw DJ. Fibromyalgia and related conditions. *Mayo Clin Proc.* 2015;90:680-692. doi: 10.1016/j.mayocp.2015.03.014
2. Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum.* 1995;38:19-28. doi: 10.1002/art.1780380104
3. Lindell L, Bergman S, Petersson IF, Jacobsson LT, Herrström P. Prevalence of fibromyalgia and chronic widespread pain. *Scand J Prim Health Care*. 2000;18:149-153. doi: 10.1080/028134300453340
4. Topbas M, Cakirbay H, Gulec H, Akgol E, Ak I, Can G. The prevalence of fibromyalgia in women aged 20-64 in Turkey. *Scand J Rheumatol.* 2005;34:140-144.
5. Turhanoğlu AD, Yilmaz Ş, Kaya S, Dursun M, Kararmaz A, Saka G. The epidemiological aspects of fibromyalgia syndrome in adults living in Turkey: a population based study. *J Musculoskelet Pain*. 2008;16:141-147.
6. Garip Y, Öztaş D, Güler T. Prevalence of fibromyalgia in Turkish geriatric population and its impact on quality of life. *Agri*. 2016;28:165-170. doi: 10.5505/agri.2016.48243
7. Mease P. Fibromyalgia syndrome: review of clinical presentation, pathogenesis, outcome measures, and treatment. *J Rheumatol Suppl.* 2005;75:6-21.
8. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. report of the multicenter criteria committee. *Arthritis Rheum.* 1990;33:160-172.
9. Sendur OF, Tastaban E, Turan Y, Ulman C. The relationship between serum trace element levels and clinical parameters in patients with fibromyalgia. *Rheumatol Int*. 2008;28:1117-1121. doi: 10.1007/s00296-008-0593-9
10. Bray TM, Bettger WJ. The physiological role of zinc as an antioxidant. *Free Radic Biol Med.* 1990;8:281-291. doi: 10.1016/0891-5849(90)90076-u
11. Powell SR. The antioxidant properties of zinc. *J Nutr.* 2000;130:1447S-1454S.
12. Barros-Neto JA, Souza-Machado A, Kraychete DC, et al. Selenium and zinc status in chronic myofascial pain: serum and erythrocyte concentrations and food intake. *PLoS One.* 2016;11:e0164302. doi: 10.1371/journal.pone.0164302
13. National Institutes of Health. Office of Dieatary Supplements. https://ods.od.nih.gov/factsheets/Zinc-HealthProfessional/. Accessed March 4, 2022.
14. Al-Gebori AM, Rajab A, Al-Osami MH, Turki KM. Levels of magnesium, zinc, calcium and copper in serum of patients with fibromyalgia syndrome. *IPMJ Iraqi Postgraduate Medical Journal. 2011;10:180-183.*
15. Wolfe F, Clauw DJ, Fitzcharles MA, et al. Revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Semin Arthritis Rheum*. 2016;46:319-329.
16. World Health Organization. Regional Office for Europe. https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi. Accessed March 4, 2022.
17. Richards KC, O'Sullivan PS, Phillips RL. Measurement of sleep in critically ill patients. *J Nurs Meas.* 2000;8:131-144.
18. Gellerstedt L, Rydell Karlsson M, Medin J, Kumlin M. Patients' self-assessed sleep as a nursing tool during hospital care: A pilot study. *Nord J Nurs Res*. 2020;40:123-129.
19. Karaman Özlü Z, Özer N. Richard-Campbell sleep questionnaire validity and reliability study. *J Turk Sleep Med*. 2015;2:29-32.
20. Altindag O, Celik H. Total antioxidant capacity and the severity of the pain in patients with fibromyalgia. *Redox Rep.* 2006;11:131-135. doi: 10.1179/135100006X116628
21. Ozgocmen S, Ozyurt H, Sogut S, Akyol O. Current concepts in the pathophysiology of fibromyalgia: the potential role of oxidative stress and nitric oxide. *Rheumatol Int.* 2006;26:585-597. doi: 10.1007/s00296-005-0078-z
22. Romano TJ, Stiller JW. Magnesium deficiency in fibromyalgia syndrome. *J Nutr Med.* 1994;4:165-167.
23. Rosborg I, Hyllén E, Lidbeck J, Nihlgård B, Gerhardsson L. Trace element pattern in patients with fibromyalgia. *Sci Total Environ*. 2007;385:20-27. doi: 10.1016/j.scitotenv.2007.05.014
24. Turki KM, Al-Osami MH, Naji RI. Zinc and selenium status in Iraqi patients with fibromyalgia syndrome. *I Jour Adv Eng Tech.* 2012;3:105-107.
25. Shukla V, Das SK, Mahdi AA, et al. Metal-induced oxidative stress level in patients with fibromyalgia syndrome and its contribution to the severity of the disease: a correlational study. *J Back Musculoskelet Rehabil.* 2021;34:319-326. doi: 10.3233/BMR-200102
26. Russell IJ, Michalek JE, Flechas JD, Abraham GE. Treatment of fibromyalgia syndrome with super malic: a randomized, double blind, placebo controlled, crossover pilot study. *J Rheumatol.* 1995;22:953-958.

27. Maes M, Mihaylova I, De Ruyter M. Lower serum zinc in chronic fatigue syndrome (CFS): relationships to immune dysfunctions and relevance for the oxidative stress status in CFS. *J Affect Disord*. 2006;90:141-147. doi: 10.1016/j.jad.2005.11.002
28. Okumus M, Ceceli E, Tuncay F, Kocaoglu S, Palulu N, Yorgancioglu ZR. The relationship between serum trace elements, vitamin B12, folic acid and clinical parameters in patients with myofascial pain syndrome. *J Back Musculoskelet Rehabil.* 2010;23:187-191. doi: 10.3233/BMR-2010-0264
29. Joustra ML, Minovic I, Janssens KAM, Bakker SJL, Rosmalen JGM. Vitamin and mineral status in chronic fatigue syndrome and fibromyalgia syndrome: A systematic review and meta-analysis. *PLoS One.* 2017;12:e0176631. doi: 10.1371/journal.pone.0176631
30. McCarthy LH, Bigal ME, Katz M, Derby C, Lipton RB. Chronic pain and obesity in elderly people: results from the Einstein aging study. *J Am Geriatr Soc.* 2009;57:115-119. doi: 10.1111/j.1532-5415.2008.02089.x
31. Yunus MB, Arslan S, Aldag JC. Relationship between body mass index and fibromyalgia features. *Scand J Rheumatol.* 2002;31:27-31. doi: 10.1080/030097402317255336
32. Fukunaka A, Fujitani Y. Role of zinc homeostasis in the pathogenesis of diabetes and obesity. *Int J Mol Sci.* 2018;19:476. doi: 10.3390/ijms19020476
33. Olechnowicz J, Tinkov A, Skalny A, Suliburska J. Zinc status is associated with inflammation, oxidative stress, lipid, and glucose metabolism. *J Physiol Sci.* 2018;68:19-31. doi: 10.1007/s12576-017-0571-7
34. Rios-Lugo MJ, Madrigal-Arellano C, Gaytán-Hernández D, Hernández-Mendoza H, Romero-Guzmán ET. Association of serum zinc levels in overweight and obesity. *Biol Trace Elem Res.* 2020;198:51-57. doi: 10.1007/s12011-020-02060-8
35. Listya H, Sulchan M, Murbawani EA, Puruhita N, Sukmadianti A. Correlation of obesity status with zinc serum levels and insulin resistance in perimenopause obese women. *DIMJ.* 2020;1:50-55.
36. Ennes Dourado Ferro F, de Sousa Lima VB, Mello Soares NR, Franciscato Cozzolino SM, do Nascimento Marreiro D. Biomarkers of metabolic syndrome and its relationship with the zinc nutritional status in obese women. *Nutr Hosp*. 2011;26:650-654. doi: 10.1590/S0212-16112011000300032
37. Zaky D, Sultan EA, Salim MF, Dawod RS. Zinc level and obesity. *Egypt J Intern Med.* 2013;25:209-212.
38. Okifuji A, Donaldson GW, Barck L, Fine PG. Relationship between fibromyalgia and obesity in pain, function, mood, and sleep. *J Pain.* 2010;11:1329-1337. doi: 10.1016/j.jpain.2010.03.006
39. Morelhão PK, Tufik S, Andersen ML. The interactions between obesity, sleep quality, and chronic pain. *J Clin Sleep Med*. 2018;14:1965-1966. doi: 10.5664/jcsm.7510
40. Ji X, Liu J. Associations between blood zinc concentrations and sleep quality in childhood: a cohort study. *Nutrients.* 2015;7:5684-5696. doi: 10.3390/nu7075247
41. Xu S, Zou D, Tang R, et al. Levels of trace blood elements associated with severe sleep disturbance in maintenance hemodialysis patients. *Sleep Breath*. 2021;25:2007-2013. doi: 10.1007/s11325-021-02336-w
42. Hajianfar H, Mollaghasemi N, Tavakoly R, Campbell MS, Mohtashamrad M, Arab A. The association between dietary zinc intake and health status, including mental health and sleep quality, among Iranian female students. *Biol Trace Elem Res.* 2021;199:1754-1761. doi: 10.1007/s12011-020-02316-3
43. Castro-Marrero J, Zaragozá MC, López-Vílchez I, et al. Effect of melatonin plus zinc supplementation on fatigue perception in myalgic encephalomyelitis/chronic fatigue syndrome: a randomized, double-blind, placebo-controlled trial. *Antioxidants (Basel)*. 2021;10:1010. doi: 10.3390/antiox10071010