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Original Article

Importance of Serum Selenium Levels in Acute Heart Failure

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ABSTRACT

Background: The role of micronutrients such as selenium is linked to the different types of cardiomyopathies. Given the paradoxes and limitations of previous studies, we designed a descriptive-analytic study with a greater sample size and more variables in Iran.

Methods: Fifty-five patients suffering from heart failure (HF) with glomerular filtration rates of 60 mL/min or higher were selected. At the onset of admission, the serum levels of selenium, proBNP, magnesium, calcium, potassium, and iron, as well as the variable of estimating prognosis (ie, 5 years' survival based on the Seattle Heart Failure Model calculator), and also a history of diabetes mellitus, hypertension, cerebrovascular accidents, cigarette use, atrial fibrillation, and previous admissions for HF, were registered. Three months later, the New York Heart Association (NYHA) functional class, the left ventricular ejection fraction, and the proBNP level were rechecked.

Results: Selenium deficiency (≤ 45µg/L) was detected in 25.4% of the patients. The mean serum level of selenium was 62 ± 24.9 µg/L, and it had no significant relationship with etiology; prognosis; the left ventricular ejection fraction; the proBNP level; the NYHA functional class; the dose of furosemide before admission; the consumption of angiotensin-converting-enzyme inhibitors/angiotensin II receptor blockers, beta-blockers, statins, and allopurinol; laboratory variables; age; sex; diabetes mellitus; hypertension; cerebrovascular accidents; atrial fibrillation; and cigarette use. Nonetheless, the mean serum level of selenium had significant reversed relationships with previous admissions for HF and potassium-sparing diuretic use (P = 0.012 and P = 0.026, respectively) (confidence interval = 95%).

Conclusions: The prevalence of selenium deficiency in our patients with HF was considerable. The mean serum level of selenium was similar in both ischemic and nonischemic groups; nevertheless, the level had no significant relationship with the majority of clinical and paraclinical variables of HF severity and prognosis. Future studies should investigate the relationship between the serum level of selenium and the precise cumulative dose of diuretics at the end of the admission process and the interaction between selenium and mineralocorticoid receptors. ***(Iranian Heart Journal 2020; 21(3): 109-118)***

KEYWORDS: Micronutrients, Selenium, Cardiomyopathy, Heart failure, Diuretic

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Congestive heart failure (CHF) is an incapacitating disease that affects 1% to 2% of the general population and still has poor prognoses despite recent advancements in the management of heart failure (HF). Mortality in the first year is between 30% and 50%, and 3 years' survival is 70%. The guideline-directed treatment of HF includes diuretics, angiotensin-converting-enzyme inhibitors/angiotensin II receptor blockers (ACEIs/ARBs), beta-blockers, and aldosterone antagonists. [1]

Aldosterone/mineralocorticoid receptors have a significant role in water and electrolyte retention and the consequent progression of salt-sensitive hypertension and linked end-organ damage. The excessive use of salt could lead to the inappropriate activation of mineralocorticoid receptors and the undesirable synergistic effects of aldosterone and salt, resulting in hypertension, cardiovascular damage, and renal dysfunction. [2]

Loss of appetite, malabsorption, older age, and frequent admissions are all factors leading to deficiency in nutrient elements in patients with HF. [1] Micronutrients and trace elements are dietary components that are not produced in the human body but are necessary for growth and disease prevention. The role of selenium, copper, and zinc in demonstrating cardiovascular diseases has been proven in previous studies. [1, 3, 4]

Selenium, as a constituent of selenoproteins, has structural and enzymatic roles. [5] The 2 main dietary forms of selenium are selenocysteine, which is derived from animal-sourced foods, and selenomethionine, which is obtained from animal-sourced foods and cereal products grown in selenium-rich soil. Nonetheless, animal-derived foods are a better dietary source for humans because selenium is necessary as an essential nutrient for animal life. [6] The recommended mean daily dose of selenium is 60 µg for men and 53 µg for women. In different countries, different absorption of selenium results in variable serum selenium levels. [7] The selenium level in agricultural products is related to the selenium content of the soil. Soil is reported to have selenium deficiency in specific regions, including Finland, New Zealand, China, and the east coast of the United States. [8] Hence, the mean serum level of selenium in different countries varies from 41.7 µg in Finland to 158.2 µg/L in Canada.[9]

In our country, Iran, although the levels of selenium in soil and water in different regions are low, the typical levels of selenium in essential crops (ie, rice in the north, wheat in the center, and dates and pistachios in the South) are relatively high. [10] In a study by Salmani [11] et al in 2013 on 58 healthy young subjects (16–32 y) in the city of Yazd in central Iran, the mean serum level of selenium was 89.4 ± 25.4 µg/L, and it was significantly higher in the male sex.

A study by Hu and Chan [12] on 10 740 Canadians revealed that the serum selenium level was higher in men, Asians, older individuals, and frequent users of nuts and vegetables, while it was lower in current smokers and frequent consumers of meat, fruit, or dairy.

The liver and kidney have a significant role in the metabolism of selenium; the excretion of selenium is mostly through urine and stool. [13] The serum levels of selenium and the linked antioxidants are decreased considerably in chronic kidney disease, especially in patients on hemodialysis. [14] The largest amount of the excretion of selenium and zinc has been recorded in patients with glomerulonephritis. [15] Urinary excretion of selenium is directly dependent on the urinary excretion of creatinine (the glomerular filtration rate) and potassium, which indicates the role of muscular mass in

selenium excretion, such that extreme muscular activity (running) increases selenium excretion, limiting the use of urinary selenium as a parameter of body selenium condition. On the other hand, urinary selenium excretion may accompany proteinuria. [16]

The metabolism of selenium is detectable in serum, whole blood, and urine; in addition, it can be determined through the activity of glutathione peroxidase in erythrocytes or platelets. [17] The most frequently used method of measuring the serum level of selenium is graphite furnace atomic absorption. [18,19] In an investigation by Muszynska et al [20] in 2012, the blood and serum levels of selenium were measured by graphite furnace atomic absorption spectroscopy (GF-AAS), and the storage of whole blood samples in −20 °C was found to be inappropriate. Moreover, it was not possible to centrifuge the serum for measurement even after the shortest time of incubation. However, for the samples stored at +4 °C, after periods of 3, 7 and, 14 days, the selenium level was higher than the initial level (7%, 11%, and 24%, respectively). On the other hand, neither the temperature nor the time of the storage of the centrifuged serum samples had any interference with the selenium level. In all the analyzed cases, Muszynska and colleagues reported that the selenium level did not differ more than 10% of the initial level.

Different studies have documented the mean serum level of selenium and its relationship with different variables (Table 1).

In the west of Iran, in 2002, Kharazi et al [25] assessed 124 patients with myocardial infarction and reported a mean serum level of selenium of 80.61 µg/L, which had no significant sexual difference and was within a range considered to be the normal level in other countries but was significantly lower than the basic serum level of selenium in Kermanshah city (104 µg/L). In a study by Arroyo et al [26] in 2006 on African-Americans with nonischemic CHF, the rates of selenium deficiency in groups of 15 patients with protracted (≥ 4 wk) CHF, 15 patients with short-term (1–2 wk) CHF, and 10 outpatients with stable compensated failure were 100%, 60%, and 90% respectively. Arroyo and colleagues concluded that selenium deficiency affected the severity of HF (in addition to causing HF). Kosar et al, [27] in a study performed in Turkey in 2006, revealed similarities in terms of serum selenium levels between ischemic HF and idiopathic HF groups.

Some interventional studies have evaluated the effects of selenium supplements. Witte et al [28] in 2005 reported that the consumption of multi-mineral and vitamin capsules improved left ventricular (LV) volumes and the left ventricular ejection fraction (LVEF). Hiraoka et al [29] in 2013 concluded that the consumption of selenium supplements improved LVEF. Raygan et al [30] in 2018 reported that selenium supplements were beneficial for cardiometabolic risk markers. Rees et al [31] in 2013 conducted a systematic review and found that the consumption of selenium supplements had no preventive effects against mortality from cardiovascular diseases.

In view of the paradoxes and limitations of the previous studies, we designed this current descriptive-analytic study with a greater sample volume and more variables in Iran.

Table 1: Studies reporting the mean serum level of selenium and its relationship with various variables

Reference Number	Study	Year	Region	Group (n)	Mean Serum Level of Selenium (µg/L)	Relation Between Groups
19	Navarro	1995	Spain	Healthy (135)	74.90	----
11	Salmani	2013	Center of Iran (Yazd)	Healthy young (58)	89.4±25.4	Higher in men than women (significant)
21	da Cunha	2002	Brazil	DCM (30)	72.3±14.3	No significant relationship with LVEF
				Control (30)	73.2±9.9	
22	Oster	1983	---	CHF (20)	47.8±16.2	Significant relationship with LVEF
				Control	80.1±13.2	
23	Auzepy	1987	France	CHF (48)	68.53±2.26	Significant difference between CHF and control (but not with MI)
				Control (48)	84.73±1.79	
				MI (31)	73.55±2.33	
24	Salonen	1982	Finland	MI	51.8	Significant difference with control
				Control	55.3	
25	Kharazi	2002	West of Iran (Kermanshah)	MI (124)	80.61	Significant difference with the city center
				City center	104	

LVEF, Left ventricular ejection fraction; DCM, Dilated cardiomyopathy; CHF, Congestive heart failure; MI, Myocardial infarction

METHODS

The present study recruited 55 patients with HF (either known case or newly diagnosed) admitted to Rajaie Cardiovascular Medical and Research Center (RHC) in 2018. RHC is a tertiary referral center in the Iranian capital, Tehran. Patients who had a glomerular filtration rate of less than 60 mL/min were excluded. The etiology of HF was divided into ischemic and idiopathic (nonischemic) according to angiography reports.

At the onset of admission, the serum levels of selenium (normal: 46–143 µg/L), proBNP (pg/mL), magnesium (normal: 1.8–2.6 mg/dL), calcium (normal: 8.5–10.5 mg/dL), potassium (normal: 3.8–5.6 meq/L), and iron (µg/dL) were measured and recorded. Additionally, the variables pertaining to the estimation of prognosis (ie, percentage of 5 years' survival based on the Seattle Heart Failure Model [SHFM] calculator) and a history of diabetes mellitus, hypertension, cerebrovascular accidents, cigarette use, and atrial fibrillation rhythm in electrocardiography (ECG) were all registered in checklists. The variables relating to the estimation of 5 years' survival based on the SHFM (Est-5y-survival-SHFM) comprised LVEF (according to echocardiography at the onset of admission); the New York Heart Association (NYHA) functional class (ie, I/II/III/IV); etiology (ischemic/nonischemic); age (y); sex (male/female); weight (kg); the dose of the loop diuretic used (mg); the use or non-use of potassium-sparing diuretics, ACEIs/ARBs, beta-blockers, statins, and allopurinol; systolic blood pressure (mm Hg); a history of device implantation (ie, none, implantable cardioverter-defibrillators, cardiac resynchronization therapy, and cardiac resynchronization therapy devices); intraventricular conduction delays in ECG (ie, narrow QRS, left bundle branch block, and right bundle branch block); hemoglobin levels (g/dL); the white blood cell count (lymphocyte percentage); serum uric acid

levels (normal: 3.6–8.2 mg/dL in men and 2.3–6.1 mg/dL in women); total serum cholesterol (mg/dL) levels; and the serum level of sodium (136–146 meq/L). Eventually, the Est-5y-survival-SHFM percentage was graded to 3 groups: high-risk (≤ 69%), intermediate-risk (70–85%), and low-risk (≥ 86%) in accordance with a study by Stefanescu et al [32] in 2014. LVEF was graded to 3 groups (≤ 19%, 20–29%, and ≥ 30% [30–40%]). The NYHA functional class, LVEF, and the serum level of proBNP were rechecked 3 months later in the same patients.

The goals of the study were to determine the prevalence of serum selenium deficiency and to evaluate the analytic relationship between the serum level of selenium and the abovementioned variables.

Routine blood samples were taken of each patient at the onset of admission and were stored in a 4 °C refrigerator. The measurement of the serum level of selenium via the atomic absorption method was done on the same samples during a 24-hour period after sampling.

Following data collection, the analysis was carried out using the SPSS software with a confidence interval (CI) of 5%. The cost of the project was provided by the research team, and no excess financial cost was imposed on the patients. Informed consent was obtained from each patient. One of the limitations of our study was neglecting the cumulative dose of furosemide received during hospitalization. (Because the samples were gathered at the onset of admission and not at the end of the admission process.) Another weakness of note is that we did not evaluate daily dietary selenium. (Because the geographic dispersion and diet diversity of patients referred to RHC is high).

RESULTS

First, the normal distribution of the quantitative variables was confirmed by the one-sample Kolmogorov–Smirnov test. Among the 55 patients, 14 (25.4%) had selenium deficiency. A description of the quantitative variables, including the percentage of the Est-5y-suvival-SHFM, the percentage of LVEF (at the onset of admission and 3 months later), the proBNP level (at the onset of admission and 3 months later), and the dose of furosemide used before admission, is presented in Table 2. The correlations between the mean serum level of selenium and the quantitative variables had no statistical significance; there was only a borderline positive correlation with age ($P = 0.085$, $r = 0.234$).

The frequencies of the qualitative variables, including etiology, the NYHA functional class (at the onset of admission and 3 months later), the grade of LVEF (at the onset of admission and 3 months later), the grade of the Est-5y-survival-SHFM, sex, previous admissions, and potassium-sparing diuretic use, are presented in Table 3. The analytic relationship between the mean serum level of selenium and the majority of the quantitative variables had no statistical significance; there was only a significantly reversed relationship between the mean serum level of selenium and previous admissions and potassium-sparing diuretic use ($P = 0.012$ and $P = 0.026$, respectively). During the analysis of the relationship between the mean serum level of selenium and the Est-5y-survival-SHF, the low-risk group (which had just 1 patient) was removed from the one-way analysis.

DISCUSSION

As was presented in the results, the prevalence of selenium deficiency (≤ 45µg/L) among our 55 patients was considerable (25.4%). Our findings are in stark contrast with the results of the study by Arroyo et al [26] in 2006 in the United States (100%, 60%, and 90%), which had a lower sample volume (40 patients). [26]

The mean and the standard deviation of the serum level of selenium was 62 ± 23.9, which is close to the result of a study by Auzepy et al [23] in 1987 on 48 patients with CHF in France (68.53 ± 2.26) but different from the result of a study by Oster et al [22] on 20 patients with CHF in 1983 (47.8 ± 16.2) and the result of a study by da Cunha et al [21] in 2002 on 30 patients with dilated cardiomyopathy (72.3 ± 14.3). Furthermore, in our study, the mean serum level of selenium in the ischemic and idiopathic groups had no significant difference, which is in agreement with the study by Kosar et al [27] in 2006 in Turkey. It is worthy of note that the mean serum level of selenium in healthy Iranians has thus far been reported only in 1 study: Salmani et al [11] in 2013 on 58 healthy young subjects from the center of Iran (89.4 ± 25.4).

Table 2: Description of the quantitative variables and their relationships with the serum level of selenium

	Mean ± SD (Min-Max)	Correlation With the Serum Level of Selenium
Selenium (µg/L)	62.1 ± 23.9 (7.3–128.5)	----------
Est-5y-survival-SHFM (%)	34.3 ± 26.1 (0–89)	*P*=0.992 *r*=0.001
LVEF (%)	17.1 ± 9.8 (5–40)	*P*=0.436 *r*=0.107
LVEF 3 months later (%)	17.2 ± 10.7 (5–50)	*P*=0.445 *r*=0.105
proBNP (pg/mL)	6341.6 ± 6114.5 (116–35000)	*P*=0.223 *r*= −0.167
proBNP 3 months later (pg/mL)	5428.6 ± 5906.8 (101–23346)	*P*=0.224 *r*= −0.167
Age (y)	50.1 ± 15.4 (20–93)	*P*=0.085 *r*=0.234
SBP (mm Hg)	105 ± 18.1 (60–153)	*P*=0.845 *r*=0.027
Heart rate (per minutes)	85.1 ± 15.5 (60–130)	*P*=0.849 *r*=−0.026
Weight (kg)	73.4 ± 15.2 (42–110)	*P*=0.364 *r*=0.125
Hemoglobin (g/dL)	13.1 ± 1.9 (8.5–17.9)	*P*=0.361 *r*=−0.126
White blood cells	7383.9 ± 1928.5 (3500–13110)	*P*=0.441 *r*=0.106
Lymphocyte (%)	25.6 ± 12.8 (6–85)	*P*=0.309 *r*=−0.140
Total cholesterol (mg/dL)	126.1 ± 34.1 (65–231)	*P*=0.179 *r*=0.184
Uric acid (mg/dL)	7.8 ± 2.3 (3.1–13.4)	*P*=0.119 *r*=−0.213
Creatinine	1 ± 0.1 (0.6–1.4)	*P*=0.297 *r*=0.143
Blood urea nitrogen	28.3 ± 12.4 (11–63)	*P*=0.895 *r*=−0.018
Sodium (meq/L)	133.8 ± 6.2 (110–145)	*P*=0.733 *r*=0.047
Potassium (meq/L)	4.1 ± 0.4 (2.7–5.3)	*P*=0.160 *r*=0.192
Magnesium (mg/dL)	2.2 ± 0.4 (1.6–3.6)	*P*=0.325 *r*=−0.135
Calcium (mg/dL)	8.5 ± 0.7 (7.1–10.5)	*P*=0.792 *r*=−0.036
Iron (µg/dL)	83.3 ± 55.9 (16–412)	*P*=0.092 *r*=−0.230
Furosemide dose (mg/d)	103.2 ± 67.6 (0–240)	*P*=0.515 *r*=0.090
Metolazone dose (mg/d)	0.2 ± 0.5 (0– 2.5)	*P*=0.610 *r*=0.070
Hydrochlorothiazide dose (mg/d)	0.6 ± 3.7 (0– 25)	*P*=0.355 *r*=−0.127

Est-5y-survival-SHFM, Estimation of 5 years' survival based on the Seattle Heart Failure Model; LVEF, Left ventricular ejection fraction

Table 3: Frequencies of the qualitative variables and their relationships with the serum level of selenium

	Frequency (%)	Mean ± SD of the Serum Level of Selenium	Relationship With the Serum Level of Selenium
Etiology: ischemic	18 (32.7%)	61 ± 24.9	*P*=0.813
Etiology: idiopathic	37 (67.3%)	62.6 ± 23.7	
NYHA FC – II	10 (18.2%)	70.2 ± 22.4	*P*=0.491
NYHA FC – III	34 (61.8%)	59.8 ± 26.4	
NYHA FC – IV	11 (20%)	61.7 ± 16.0	
NYHA FC– I 3 months later	5 (9.1%)	60.8 ± 32.7	*P*=0.140
NYHA FC – II 3 months later	28 (50.9%)	57.4 ± 20.7	
NYHA FC – III 3 months later	13 (23.6%)	75.3 ± 29.4	
NYHA FC – IV 3 months later	9 (16.4%)	57.1 ± 23.9	
LVEF ≤19%	36 (65.5%)	59.3 ± 21.3	*P*=0.478
LVEF 20-29%	8 (14.5%)	65 ± 19.2	
LVEF ≥30%	11 (20%)	69 ± 33.9	
LVEF ≤19% 3 months later	37 (67.3%)	59.2 ± 21	*P*=0.390
LVEF 20-29% 3 months later	5 (9.1%)	73.2 ± 18.2	
LVEF ≥30% 3 months later	13 (23.6%)	65.8 ± 32.3	
High-risk Est-5y-survival-SHFM	50 (90.9%)	61.3 ± 24	*P*=0.675 (low-risk group removed)
Intermediate-risk Est-5y-survival-SHFM	4 (7.3%)	72.5 ± 26.8	
Low-risk Est-5y-survival-SHFM	1 (1.8%)	61	
Male Sex	33 (60%)	62.9 ± 24.3	*P*=0.759
Female Sex	22 (40%)	60.8 ± 23.8	
Positive previous admission	45 (81.8%)	58.3 ± 21.7	*P*=0.012
No previous admission	10 (18.2%)	79.0 ± 27.4	
Positive smoking	13 (23.6%)	59.0 ± 17.3	*P*=0.598
No smoking	42 (76.4%)	63.0 ± 25.7	
Positive diabetes mellitus	8 (14.5%)	66.1 ± 31.8	*P*=0.608
No diabetes mellitus	47 (85.5%)	61.4 ± 22.7	
Positive hypertension	12 (21.8%)	66.5 ± 33.6	*P*=0.470
No hypertension	43 (78.2%)	60.8 ± 20.8	
Positive cerebrovascular accidents	3 (5.5%)	74.2 ± 18.6	*P*=0.371
No cerebrovascular accidents	52 (94.5%)	61.4 ± 24.1	
Positive atrial fibrillation	5 (9.1%)	53.3 ± 20.0	*P*=0.398
No atrial fibrillation	50 (90.9%)	62.9 ± 24.3	
Positive use of ACEI or ARB	36 (65.5%)	67.4 ± 23.9	*P*=0.232
No use of ACEI or ARB	19 (34.5%)	59.2 ± 23.8	
Positive use of potassium-sparing diuretics	49 (89.1%)	59.6 ± 23.6	*P*=0.026
No use of potassium-sparing diuretics	6 (10.9%)	82.5 ± 16	
Positive use of beta-blockers	48 (87.3%)	61.4 ± 24.5	*P*=0.609
No use of beta-blockers	7 (12.7%)	66.5 ± 20.6	
Positive use of allopurinol	22 (40%)	59.4 ± 16.4	*P*=0.498
No use of allopurinol	33 (60%)	63.9 ± 27.9	
Positive use of statins	9 (16.4%)	54.7 ± 33.0	*P*=0.315
No use of statins	46 (83.6%)	63.5 ± 21.9	

NYHA FC, New York Heart Association functional class; Est-5y-survival-SHFM, Estimation of 5 years' survival based on the Seattle Heart Failure Model; LVEF, Left ventricular ejection fraction; ACEI, Angiotensin-converting-enzyme inhibitor; ARB, Angiotensin II receptor blocker

The age of the patients in our study was 20 to 93 years old with a mean of 50.1 years old. Men accounted for 60% of the study population. In addition, 32.7% of the patients had an ischemic etiology, 61.8% were in the NYHA functional class III,

65.5% had LVEF of 19% or lower, 90.9% had high-risk Est-5y-survival-SHFM, 81.8% had previous admissions for HF, 14.5% had diabetes mellitus, 5.5% had a history of cerebrovascular accidents, 23.6% were cigarette smokers, and 9.1% had a history of atrial fibrillation rhythm in ECG.

Because RHC is a tertiary referral heart center in Iran, most of the patients recruited in the current investigation were on the guideline-directed treatment of HF (ie, loop diuretics, ACEIs/ARBs, beta-blockers, and mineralocorticoid receptor antagonists). Still, we had 3 patients with new (*de novo*) HF under no treatment. With respect to drug discontinuation without consultation with the treating physician, 3 patients discontinued potassium-sparing diuretics, 3 patients discontinued beta-blockers, and 3 patients discontinued ACEIs/ARBs. Moreover, 1 patient discontinued beta-blockers and 13 patients discontinued ACEIs/ARBs because of decreased systolic blood pressure.

The fact that we found no significant relationship between the mean serum level of selenium and LVEF is in agreement with the study by da Cunha et al [21] but in contrast with the study by Oster et al. [22] Additionally, the mean serum level of selenium had no significant relationships with etiology; the NYHA functional class; proBNP; Est-5y-survival-SHFM; sex (in contrast with some studies) [11,12]; diabetes mellitus; cerebrovascular accidents; cigarette use (in contrast with the study by Hu and Chan) [12]; atrial fibrillation rhythm; the consumption of ACEIs/ARBs, beta-blockers, statins, and allopurinol; the dose of furosemide used; the serum levels of iron, calcium, magnesium, potassium, sodium, creatinine, uric acid, and hemoglobin; the white blood cell count; the lymphocyte percentage; systolic blood pressure; and weight. A possible explanation for the absence of a relationship between the dose of furosemide used and the mean serum level of selenium was that we gathered the samples at the onset of admission, not at the end of the admission process, precluding the assessment of the cumulative dose of furosemide used.

The mean serum level of selenium had a borderline positive relationship with age, which is in agreement with the finding of the study by Hu and Chan, [12] who also reported higher serum selenium levels in older patients.

The mean serum level of selenium had a significant reversed relationship with previous admissions for HF and potassium-sparing diuretic use. It is likely that the lower serum levels of selenium in our patients with previous admissions were in consequence of impaired gastrointestinal absorption due to more congestion and the reduced perfusion of the gastrointestinal system. It might also have been a result of the consumption of more doses of furosemide (intravenously) during previous admissions, which would once again highlight our failure to measure the serum level of selenium at the end of the admission process (in addition to the onset of admission). Future investigations should, therefore, take heed of this significant issue. Furthermore, the lower serum level of selenium in our potassium-sparing diuretic users alongside the absence of a relationship between the serum level of selenium and the serum level of potassium raises the suspicion that potassium-sparing diuretics have selenium excretory effects. Be that as it may, we found no study on the interaction between mineralocorticoid receptors and selenium, which can be considered an issue to be used as an endpoint in future studies.

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