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ORIGINAL ARTICLE

THE EVALUATION OF ZINC, COPPER, AND SELENIUM TEST RESULTS IN GERIATRIC PATIENTS: THE FIVE-YEAR EXPERIENCE

Abstract

Introduction: People aged 65 and above constitute 9% of the world's population and 9.1% of the population in Türkiye. Age-related changes in trace element content occur. In the present study, researchers aimed to evaluate the zinc, copper, and selenium test results in geriatric patients.

Material and Methods: Data on geriatric patients' serum zinc, copper, and selenium tests between 01/02/2019 and 28/02/2024 were acquired from the laboratory information system at Ankara Bilkent City Hospital. Zinc and copper tests were performed using the Shimadzu AAS 7000 Atomic Absorption Spectrophotometer device, and selenium tests were performed using the Agilent 7700 Inductively Coupled Plasma—Mass Spectrometer device. Patients aged 65 and over were evaluated in age groups (youngest-olds: 64 to 74 years, middle-olds: 75 to 84 years, and oldest-olds: 85 years and over), gender, and preliminary diagnoses. Diagnoses were presented with International Classification of Diseases codes.

Results: 4231 zinc, 2180 copper, and 135 selenium test results were evaluated. Zinc levels grouped according to reference ranges showed a statistically significant difference among age intervals ($p < 0.001$), while no statistically significant differences were observed for copper tests ($p = 0.790$) and selenium tests ($p = 0.700$). Age intervals of copper showed a statistically significant difference among genders ($p = 0.019$), while no statistically significant differences were observed for zinc ($p = 0.657$) and selenium ($p = 0.326$) tests.

Conclusion: We evaluated zinc, copper, and selenium levels in geriatric patients according to different age groups, ICD codes, and gender. Our findings may serve as a useful reference for future research.

Keywords: Zinc; Copper; Selenium; Trace Elements; Aging; International Classification of Diseases.

INTRODUCTION

Aging in the human body occurs over time (1). People aged 65 and above constitute 9% of the world's population and 9.1% of the population in Türkiye (2). The dynamic, physiological, and continuous aging process is complex. In biological aging, changes occur progressively in the metabolism and physicochemical properties of cells as age increases. Impairments in cell self-regulation and regeneration can lead to structural changes in the cell and functional disorders in tissues and organs (3). Chronic inflammation, progenitor cell dysfunction, and damaged macromolecules may play a role in the cellular and molecular changes that occur with aging (4). Furthermore, age-related changes in trace element content occur (5).

Trace elements are dietary minerals, required in trace amounts for the body's physiological functions. In the body, each trace element constitutes less than 0.01% of body mass, while the total amount of all trace elements is less than 1% of total body mass (6). Trace elements have the following properties: They are found in living beings, and interact with living substances, and additionally, the biological effects that occur due to lower levels of the optimum levels of trace elements can be reversed when they reach their optimum levels (7). Trace elements are components of certain enzymes and structural factors that play roles in preventing nutritional deficiencies, chronic diseases, and in supporting immunity, regulating gene expression, and antioxidant defense (6).

Zinc (Zn) is involved in protein, lipid, and nucleic acid metabolism, immune system functions, wound repair, and activation of macrophages, neutrophils, and natural killer cells in the human body. Zn cannot be synthesized in the human body, and its adequate levels must be maintained in humans. Hereditary malabsorption, inadequate zinc intake, and increased metabolic requirements can cause Zn deficiency. Zn deficiency can be seen in Crohn's disease, pancreatic insufficiency, small intestinal malabsorption, anorexia nervosa, short bowel syndrome, certain strict vegetarian diets, and hookworm infections (8).

It has been suggested that Zn deficiency might be prevalent in elderly people. There are also studies showing a relationship between zinc deficiency and various diseases in the elderly (9).

Copper (Cu), a transition element, is abundant in the human body. This trace element is necessary for collagen synthesis, skin pigmentation, oxygen and iron metabolism, and the synthesis of some neurotransmitters. It also plays a role in antioxidant defense. It is involved in many cellular pathways. It is important for neuronal functions. Both excessive high and low Cu levels are harmful to humans. (10).

Selenium (Se) has antioxidant and anti-inflammatory properties. It plays a role in the production of active thyroid hormone. Low Se levels lead to an increased risk of death, weakening of the immune system, and decline in cognitive functions. High Se levels have antiviral effects, positively affect reproductive system functions in women and men, and reduce the risk of autoimmune thyroid disease (11). The strategic status of Se against aging and age-related diseases is still unclear (12).

In this study, the aim was to evaluate serum zinc, copper, and selenium levels in geriatric patients admitted to Ankara Bilkent City Hospital between 01/02/2019 and 28/02/2024. To the best of our knowledge, this is the first retrospective study to evaluate serum Zn, Cu, and Se levels of geriatric patients across different age groups and genders, using five years of data.

MATERIALS AND METHOD

The present study included serum Zn, Cu, and Se test results of patients aged 65 and over. Disease diagnoses are expressed with the International Statistical Classification of Diseases and Related Health Problems codes (ICD) in the Ankara Bilkent City Hospital laboratory information system.

For each test, only the first result of each patient was included. In this retrospective study, all the evaluations were conducted according to gender and age groups, including the ICD codes (13).

In our study, patients aged 65 and over were evaluated in three groups according to their ages, based on the study conducted by Lee et al. (14). The age groups in our study were as follows: youngest-olds aged between 64 and 74 years, middle-olds aged between 75 and 84 years, and oldest-olds aged 85 years and over. For the population included in our study, the reference ranges of Zn and Se do not vary according to gender, and they are as follows: 70-120 µg/dL for Zn and 63-163 µg/L for Se. The reference range of Cu is 80-155 µg/dL for females and 70-140 µg/dL for males.

Samples were taken into gel-free tubes for zinc and copper tests and into trace element tubes for selenium tests. In the present study, before the analyses of trace elements the devices were first calibrated. Then, internal quality controls were performed for each test. The analysis was performed after biochemistry experts found the internal quality controls appropriate. External quality controls for the tests were performed at periodic intervals depending on the test. The measurement procedure for each of the serum Cu and serum Zn tests was the same and was as follows: A 500 µL serum sample was taken, diluted to 10 mL with distilled water, and measured using the flame atomic absorption spectrophotometer method with the Shimadzu AAS 7000 Atomic Absorption Spectrophotometer device. Serum Se tests were performed at the external laboratory contracted with our hospital using the Agilent 7700 Inductively Coupled Plasma—Mass Spectrometer device.

All the data registered between 01/02/2019 and 28/02/2024 were acquired from the laboratory information system of Ankara Bilkent City Hospital. Ethics committee approval was obtained from Ankara Bilkent City Hospital's Ethics Committee (Number: TABED 2-24-448, Date: 04/09/2024). All the researchers worked in line with the Helsinki Declaration in every process of the present study.

Statistical Analysis

Frequency, percent, median, and interquartile ranges (IQR) were used to express the data. Statistical analyses were performed with Chi-square and Kruskal-Wallis tests. A p-value < 0.05 was regarded as statistically significant. Statistical analyses were performed with IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA).

RESULTS

The present study included the data of geriatric patients' serum zinc, copper, and selenium tests, completed between 01/02/2019 and 28/02/2024, and available in the hospital laboratory information system. A total of 4231 Zn, 2180 Cu, and 135 Se test results were evaluated. The quantitative variables are presented in Table 1.

The data of serum Zn, Cu, and Se tests among age intervals are presented in Table 2. Only serum Zn levels grouped according to reference ranges showed a statistically significant difference among age intervals ($p < 0.001$), while no statistically significant differences were observed for Cu ($p = 0.790$) and Se ($p = 0.700$) tests (Table 2).

The data of serum Zn, Cu, and Se tests across age intervals by gender are presented in Table 3. Only the age intervals of Cu showed a statistically significant difference among genders ($p = 0.019$), while no statistically significant differences were observed for the Zn ($p = 0.657$) and Se ($p = 0.326$) tests (Table 3).

In the present study, preliminary diagnoses were grouped and presented with ICD codes. The numbers and percentages of the ICD codes among the reference intervals of Zn, Cu, and Se are reported (Table 4).

Table 1. Quantitative Variables

	Zn (µg/dL)		Cu (µg/dL)		Se (µg/L)	
	N	(%)	N	(%)	N	(%)
Gender						
Female	2526	(59.7)	1146	(52.6)	98	(72.6)
Male	1705	(40.3)	1034	(47.4)	37	(27.4)
Age (Years)						
65-74	2766	(65.4)	1389	(63.7)	97	(71.8)
74-84	1173	(27.7)	636	(29.2)	34	(25.2)
85 and over	292	(6.9)	155	(7.1)	4	(3)
Test Results						
Below the Reference Range	390	(9.2)	286	(13.1)	23	(17)
Within the Reference Range	3720	(87.9)	1858	(85.2)	111	(82.3)
Above the Reference Range	121	(2.9)	36	(1.7)	1	(0.7)

Zn: Zinc, Cu: Copper, Se: Selenium

Table 2. Serum Zn, Cu, and Se Test Data For Age Intervals

		Age Intervals (years)						p
		65-74		75-84		85 and over		
		N	(%)	N	(%)	N	(%)	
Zn (µg/dL)	Below the Reference Range	195	(7.05)	140	(11.9)	55	(18.8)	<0.001*
	Within the Reference Range	2482	(89.73)	1005	(85.7)	233	(79.8)	
	Above the Reference Range	89	(3.22)	28	(2.4)	4	(1.4)	
Cu (µg/dL)	Below the Reference Range	186	(13.3)	82	(12.9)	18	(11.6)	0.790
	Within the Reference Range	1180	(85.0)	542	(85.2)	136	(87.7)	
	Above the Reference Range	23	(1.7)	12	(1.9)	1	(0.7)	
Se (µg/L)	Below the Reference Range	12	(12.4)	10	(29.4)	1	(25)	0.700
	Within the Reference Range	85	(87.6)	23	(67.7)	3	(75)	
	Above the Reference Range	0	(0)	1	(2.9)	0	(0)	

p: Chi-square test, *: Statistical significance, Zn: Zinc, Cu: Copper, Se: Selenium

Table 3. Serum Zn, Cu, and Se Tests for Age Intervals with respect to Gender

		Gender				p
		Female		Male		
	Age Intervals (years)	N	(%)	N	(%)	
Zn (µg/dL)	65-74	1660	65.7	1106	64.9	0.657
	75-84	688	27.2	485	28.4	
	85 and over	178	7.0	114	6.7	
Cu (µg/dL)	65-74	702	61.3	687	66.4	0.019*
	75-84	350	30.5	286	27.7	
	85 and over	94	8.2	61	5.9	
Se (µg/L)	65-74	67	68.3	30	81.1	0.326
	74-84	28	28.6	6	16.2	
	85 and over	3	3.1	1	2.7	

p: Chi-square test, *: Statistical significance, Zn: Zinc, Cu: Copper, Se: Selenium

Table 4. Preliminary Diagnosis of Serum Zn, Cu, and Se Tests

Zn Tests								
Below the Reference Range			Within the Reference Range			Above the Reference Range		
ICD Codes	N	%	ICD Codes	N	%	ICD Codes	N	%
ICD 1	13	3.3	ICD 1	41	1.1	ICD 1	1	0.8
ICD 2	25	6.4	ICD 2	133	3.6	ICD 2	6	5.0
ICD 3	21	5.4	ICD 3	101	2.7	ICD 3	2	1.7
ICD 4	79	20.3	ICD 4	1108	29.8	ICD 4	36	29.8
ICD 5	5	1.3	ICD 5	33	0.9	ICD 6	2	1.7
ICD 6	18	4.6	ICD 6	105	2.8	ICD 7	1	0.8
ICD 7	5	1.3	ICD 7	34	0.9	ICD 9	10	8.3
ICD 9	21	5.4	ICD 8	10	0.3	ICD 11	8	6.6
ICD 10	6	1.5	ICD 9	144	3.9	ICD 12	3	2.5
ICD 11	21	5.4	ICD 10	37	1.0	ICD 13	11	9.1
ICD 12	8	2.1	ICD 11	278	7.5	ICD 14	5	4.1
ICD 13	21	5.4	ICD 12	102	2.7	ICD 18	17	14.0
ICD 14	10	2.6	ICD 13	311	8.4	ICD 21	19	15.7
ICD 18	58	14.9	ICD 14	81	2.2			
ICD 19	4	1.0	ICD 16	1	0.0			
ICD 20	2	0.5	ICD 18	383	10.3			
ICD 21	72	18.5	ICD 19	5	0.1			
ICD 22	1	0.3	ICD 20	5	0.1			
			ICD 21	795	21.4			
			ICD 22	13	0.3			

Table 4. Continued...

Cu Tests								
Below the Reference Range			**Within the Reference Range**			**Above the Reference Range**		
ICD Codes	**N**	**%**	**ICD Codes**	**N**	**%**	**ICD Codes**	**N**	**%**
ICD 1	15	5.2	ICD 1	13	0.7	ICD 1	1	2.8
ICD 2	16	5.6	ICD 2	117	6.3	ICD 2	4	11.1
ICD 3	5	1.7	ICD 3	33	1.8	ICD 3	1	2.8
ICD 4	34	11.9	ICD 4	235	12.6	ICD 4	1	2.8
ICD 5	6	2.1	ICD 5	22	1.2	ICD 6	3	8.3
ICD 6	54	18.9	ICD 6	247	13.3	ICD 9	3	8.3
ICD 7	4	1.4	ICD 7	22	1.2	ICD 10	1	2.8
ICD 9	13	4.5	ICD 8	2	0.1	ICD 11	1	2.8
ICD 10	2	0.7	ICD 9	73	3.9	ICD 12	2	5.6
ICD 11	18	6.3	ICD 10	15	0.8	ICD 18	11	30.6
ICD 12	3	1.0	ICD 11	151	8.1	ICD 21	8	22.2
ICD 13	13	4.5	ICD 12	4	0.2			
ICD 14	3	1.0	ICD 13	116	6.2			
ICD 18	55	19.2	ICD 14	35	1.9			
ICD 21	45	15.7	ICD 17	1	0.1			
			ICD 18	449	24.2			
			ICD 19	3	0.2			
			ICD 20	2	0.1			
			ICD 21	306	16.5			
			ICD 22	12	0.6			
Se Tests								
Below the Reference Range			**Within the Reference Range**			**Above the Reference Range**		
ICD Codes	**N**	**%**	**ICD Codes**	**N**	**%**	**ICD Codes**	**N**	**%**
ICD 2	1	4.3	ICD 2	2	1.8	ICD 21	1	100
ICD 3	2	8.7	ICD 3	9	8.1			
ICD 4	7	30.4	ICD 4	43	38.7			
ICD 6	1	4.3	ICD 6	4	3.6			
ICD 8	1	4.3	ICD 7	4	3.6			
ICD 13	2	8.7	ICD 8	3	2.7			
ICD 14	1	4.3	ICD 9	1	0.9			
ICD 21	8	34.8	ICD 11	1	0.9			
			ICD 12	1	0.9			
			ICD 13	7	6.3			
			ICD 14	2	1.8			
			ICD 18	7	6.3			
			ICD 21	27	24.3			

Zn: Zinc, Cu: Copper, Se: Selenium, ICD: International Classification of Diseases

DISCUSSION

Zinc reference ranges do not differ by gender but do differ by age. Normal zinc values by age are as follows: 26-141 µg/dL for newborns and 6 months, 29-131 µg/dL for 6-11 months, 31-115 µg/dL for 1-4 years, 48-119 µg/dL for 4-5 years, 48-129 µg/dL for 6-9 years, 25-148 µg/dL for 10-13 years, 46-130 µg/dL for 14-17 years, 70-120 µg/dL for 18 and over. Zinc levels may increase in anemia, atherosclerosis, and coronary heart disease, while they may decrease in diabetes mellitus, cirrhosis, acrodermatitis enteropathica, nephrotic syndrome, and myocardial infarction (15). The copper reference range is 20-70 µg/dL for males and females aged ≤6 months, 90-190 µg/dL for 7 months-18 years. It is 70-140 µg/dL for males aged ≥19 years and 80-155 µg/dL for females aged ≥19 years. Copper levels increase in anemia, leukemia, lymphoma, hemochromatosis, and infection, and decrease in chronic diarrhea, Menkes disease, and Kwashiorkor (15). In our hospital laboratory, the selenium reference range is stated as 40-103 µg/L for 0-4 years, 55-134 µg/L for 4-16 years, and 63-160 µg/L for 16-110 years.

Zn is a trace element that has structural and catalytic functions for many proteins, enzymes, and transcription factors. It also has roles in cell proliferation and homeostatic processes. Zn deficiency may be involved in the etiology of atherosclerosis, nervous system diseases, and cancer (16). It has been stated that low zinc levels may be related to poor metabolic status (17). Our study was in line with previous studies (16, 17). Zn levels lower than its reference range were observed in various diseases, including ICD 4 (Endocrine, nutritional, and metabolic diseases) (N = 79, 20.3%), ICD 21 (Factors influencing health status and contact with health services) (N = 72, 18.5%), ICD 18 (Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified) (N = 58, 14.9%), and others (Table 4). Long-term use of zinc preparations causes suppression of the immune system, a decrease in high-density lipoprotein levels, anemia, and possible genitourinary complications (18). In the present study, Zn levels higher than its reference range were observed in diverse diseases, and they were as follows: ICD 4 (N = 36, 29.8%), ICD 21 (N = 19, 15.7%), and ICD 18 (N = 17, 14.0%).

In a study conducted by Marcellini et al., which included results from five European countries, it was stated that 31% of people aged 60 and over had Zn deficiency (19). The study by Yasuda and Tsutsui indicated that Zn deficiency increases with age, with 20-30% of the elderly being at risk for this condition (20). Our results were not in line with Yasuda and Tsutsui's study. In their studies, Yasuda and Tsutsi used hair samples and the device they used for analysis was inductively coupled plasma mass spectrometry. We used blood samples in our study and performed the analysis with an atomic absorption spectrometry device. For these reasons, our results may have differed. In our study, there was a statistical difference between Zn reference ranges and age intervals ($p < 0.001$), with the highest percentage within the reference values in each age group (Table 2). In their study, Hennigar and his colleagues reported that serum Zn concentrations were higher in men than in women (21). In the present study, no statistical difference was observed in gender among the age intervals of Zn ($p = 0.657$) (Table 3).

High copper levels observed in the elderly were significantly associated with the occurrence of mild cognitive impairment (22). It has been reported that changes in copper levels with age may be effective in the onset of Alzheimer's and Huntington's diseases. Impaired copper homeostasis is present in age-related macular degeneration, heart failure, cardiomyopathy, and diabetic retinopathy (23). In the present study, diagnoses were diverse, in line with previous studies (22, 23). However, in all reference range groups, ICD 18 was the highest (Table 4). No statistical difference was found between reference ranges and age intervals ($p = 0.790$) (Table 2), while

in each age group, females were observed in higher numbers (p = 0.019) (Table 3).

Se is found in the structure of selenoproteins and plays a role in antioxidant activity. Reactive oxygen species are among the factors that play a role in forming diseases associated with aging. While inflammation and DNA damage caused by reactive oxygen species are reduced with Se, it contributes to the lengthening of telomeres. Se preparations for supplementation are seen as a protective strategy for diseases associated with aging , however, they do not make a definitive contribution to the prevention of these diseases (12). Our results did not provide enough descriptive detail about Se levels in geriatric individuals. In the present study, no statistical differences were observed in reference ranges among age intervals (p = 0.700) (Table 2), or between age intervals and gender (p = 0.326) (Table 3). The diagnoses associated with Se results were as follows: ICD 21 (N = 8, 34.8%), ICD 4 (N = 7, 30.4%), and others in the below reference range group. For those within the reference range, ICD 4 (N = 43, 38.7%) and ICD 3 (N = 9, 8.1%) were prominent. Only ICD 21 (N = 1, 100%) appeared in the above reference range group (Table 4).

Strengths and Limitations

The strengths of the present study were as follows: inclusion of 5-year data from Ankara Bilkent City Hospital, one of the largest hospitals in Türkiye; inclusion of only the first result of each patient in the study; evaluation of disease diagnoses according to ICD codes; and evaluation of geriatric patients in three groups: youngest-old, middle-old, and oldest-old. On the other hand, our study had some definite limitations. Patient information on the presence of metallic implants, the use of synthetic hair dye, and the intake of vitamin supplements or other medications could not be included. Additionally, when evaluating disease diagnoses, only the preliminary diagnosis was used to assign the relevant ICD code.

CONCLUSION

Aging is an inevitable process, and this process brings aging-related diseases (12). Aging involves changes in trace element levels (5). Zn, Cu, and Se are involved in the formation of various diseases. Geriatric patients represent a significant portion of the patient population. Our study, which evaluated serum zinc, copper, and selenium levels in geriatric patients according to different age groups, ICD codes, and gender, may play a helpful role in future research.

Ethics Committee Approval: Ethics Committee approval was obtained from Ankara Bilkent City Hospital (Number: TABED 2-24-448, Date: 04/09/2024)

Conflict of Interest: The authors declare no conflict of interest.

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Data Availability Statement: The present study's data are available from the corresponding author upon reasonable request.

Abbreviation List:

Zn: Zinc

Cu: Copper

Se: Selenium

ICD: International Classification of Diseases

ICD 1: Certain infectious and parasitic diseases

ICD 2: Neoplasms

ICD 3: Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism

ICD 4: Endocrine, nutritional, and metabolic diseases

ICD 5: Mental and behavioral disorders

ICD 6: Diseases of the nervous system

ICD 7: Diseases of the eye and adnexa

ICD 8: Diseases of the ear and mastoid process

ICD 9: Diseases of the circulatory system

ICD 10: Diseases of the respiratory system

ICD 11: Diseases of the digestive system

ICD 12: Diseases of the skin and subcutaneous tissue

ICD 13: Diseases of the musculoskeletal system and connective tissue

ICD 14: Diseases of the genitourinary system

ICD 15: Pregnancy, childbirth, and the puerperium

ICD 16: Certain conditions originating in the perinatal period

ICD 17: Congenital malformations, deformations, and chromosomal abnormalities

ICD 18: Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified

ICD 19: Injury, poisoning, and certain other consequences of external causes

ICD 20: External causes of morbidity and mortality

ICD 21: Factors influencing health status and contact with health services

ICD 22: Codes for special purposes

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