Advanced Medical Journal, Vol.11, No.1, P.239-246,2026 https://doi.org/10.56056/amj.2026.450

# Serum Zinc in Patients with Acute Ischemic Stroke

**Shram Sabah Hassan* Zana Abdulrahman Mohammed****

## Abstract

**Background and Purpose:** Stroke is one of the main causes of mortality and disability worldwide. Identifying new risk factors for stroke is crucial for its prevention. The purpose of this study was to determine whether serum zinc levels and ischemic stroke were related.

**Methods:** In this case-control study conducted in Shar Hospital in Slemani, Kurdistan Region, Iraq, between July 2023 and January 2024, 83 patients who had experienced an acute ischemic stroke and 83 age- and sex-matched controls were enrolled. Utilizing colorimetric measurement, the serum zinc levels were determined. We compared the serum zinc levels of both groups and sought relevant relationships between them and the other characteristics of the participants.

**Results:** We found that 79 out of 83 cases (95.2%) with acute ischemic stroke had low zinc levels (<70 µg/dL). The mean serum zinc levels of the cases and controls were 49.87 ± 13.43 µg/dL and 52.61 ± 19.86 µg/dL, respectively; their difference was not statistically significant (p=0.33). The severity of strokes showed a significant inverse relationship with the levels of zinc in the serum (r= -0.462, p<0.001); more severe strokes were associated with lower serum zinc levels. Additionally, there was a significant inverse relationship between the age of the stroke patients and their zinc levels (r= -0.258, p=0.02).

**Conclusion:** Our study did not support an association between serum zinc levels and the occurrence of acute ischemic stroke. However, it demonstrated that zinc levels are negatively correlated with age and stroke severity in patients with acute ischemic stroke.

**Key Words:** Ischemic stroke, Risk factor, Stroke severity, Zinc

*MBChB; neurology at Shar Hospital, Slemani, Kurdistan Region, Iraq. Email: shram.sabah@yahoo.com (corresponding author)
**MBChB, FIBMS, UEMS-EBN; assistant professor of neurology at College of Medicine, University of Slemani, Slemani, Kurdistan Region, Iraq. Email: zana.mohammed@univsul.edu.iq

## Introduction

Worldwide, stroke is the second most common cause of death.[1] In addition, acquired disability in adults is primarily caused by stroke in most regions of the world. Low- and middle-income nations bear the brunt of the global stroke burden, contributing more than 85 percent of all stroke deaths. About 87% of strokes are ischemic.[2] The traditional risk factors for stroke are advanced age, hypertension, diabetes mellitus, dyslipidemia, heart diseases, smoking, obesity, etc. Identifying new modifiable risk factors is crucial for prevention of stroke. Of all the trace elements in the body, zinc is the second most plentiful.[3] Zinc is a component of more than 300 enzymes and more than 1000 transcription factors.[4] It plays a role in numerous functions, including DNA synthesis, RNA transcription, growth, development, reproduction, maintenance of homeostasis, proper function of the immune system, and reduction of oxidative stress. It is believed that approximately 31% of people around the world are affected by zinc deficiency.[5] Zinc deficiency is known to cause many symptoms and diseases, e.g. growth retardation, gonadal hypofunction, increased susceptibility to infections (impaired immune function), delayed wound healing, hypogeusia, hyposmia, anorexia, alopecia, impaired glucose tolerance, depression, ataxia, dementia, skin disorders, increased incidence of cataracts, increased incidence of ischemic heart disease, increased carcinogenesis, etc.[6] There is uncertainty regarding the association between serum zinc levels and ischemic stroke, with different studies reporting conflicting results. A number of studies demonstrate a link between low blood zinc levels and ischemic stroke, indicating that deficiency of zinc may be a risk factor for ischemic stroke. In addition, some studies have found a link between zinc levels and stroke severity.[3,4,7-10] The vascular endothelium functions as a barrier. It provides resistance to numerous potentially pro-oxidant and toxic substances in the blood. [11] However, when the endothelium is injured, monocytes attach to it as part of the repair process. These monocytes go into the intima and, upon taking in oxidized low-density lipoprotein (LDL) particles, develop into lipid-laden macrophages, or foam cells. Over time, fatty streaks form and become atherosclerotic plaques. It is suggested that zinc may prevent oxidation of LDL and its uptake by macrophages, thus protecting against atherosclerosis. Apart from its function as an antioxidant and stabilizer of cell membranes, evidence suggests that zinc may protect the vascular endothelium in some other ways as well.[11,12] It participates in many endothelial signaling processes, some of which are essential for maintaining cell integrity. The aim of this study was to investigate the potential relationship between ischemic stroke and serum zinc levels. It also looked for any possible relationship between serum zinc levels and stroke severity, as well as the demographic characteristics of the patients.

## Patients and methods

This case-control study was carried out in Shar Teaching Hospital in Slemani, Kurdistan Region, Iraq, between July 2023 and January 2024. The cases consisted of 83 patients (46 men and 37 women) diagnosed with acute ischemic stroke on the basis of their history, clinical examination, and CT scan and/or MRI. Blood samples were taken from them within 72 hours of onset of stroke. The controls were 83 patients who presented to the hospital for other complaints and had never suffered a stroke. Both groups were matched for age and sex. The study did not include patients who were taking zinc supplements. Depending on the average of two readings, hypertension was defined as a systolic blood pressure of at least 140 mmHg and/or a diastolic blood pressure of at


https://doi.org/10.56056/amj.2026.450

least 90 mmHg, or as the self-reported use of antihypertensive drugs by the patient. The definition of diabetes mellitus included a fasting blood glucose level higher than 126 mg/dL or a non-fasting glucose level exceeding 200 mg/dL, or a patient's self-reported usage of antidiabetic drugs. Participants who smoked daily were classified as smokers. Ex-smokers and those who smoked occasionally were categorized as non-smokers. The National Institutes of Health Stroke Scale (NIHSS) was used to measure the severity of stroke. The participants, or their families in the event that they were unable to give consent, were asked for their informed consent. The ethics committee of the Kurdistan Higher Council of Medical Specialties approved the study protocol (REC number: 1320). Each participant had five milliliters of venous blood collected in a metal-free plastic tube (royal blue-top tube) and allowed to clot at room temperature for a period between 30 minutes and four hours. After that, the blood samples were centrifuged to extract the serum. The serum specimens were placed in polypropylene Eppendorf tubes and kept frozen at -40 °C until they were analyzed. The analysis was carried out with colorimetric determination using kits purchased from LTA, Italy. The cobas c 311 analyzer (Roche/Hitachi) was used. Means ± standard deviations were used to represent continuous data, and frequencies and percentages were used for categorical data. To evaluate the normal distribution of quantitative variables, the Kolmogorov-Smirnov and Shapiro-Wilk tests were utilized. The independent-samples t-test and ANOVA were used to analyze continuous variables. A chi-square test was used to evaluate categorical variables. Correlations between quantitative variables were assessed using Pearson correlation. The p values were regarded as statistically significant if they were less than 0.05. Version 21 of SPSS was utilized to perform the statistical analyses.

## Results

In our study, we had 83 cases of acute ischemic stroke (46 men and 37 women) and 83 age- and sex-matched controls. The participants' demographic details are displayed in Table (1). The mean age of both groups was 65.93 ± 12.43 years. In each group, there were 35 participants under the age of 65 years and 48 participants aged 65 years or over. A significantly larger number of cases had hypertension and a family history of stroke compared to the controls (71 vs 39, p= <0.001; 23 vs 9, p=0.01, respectively). Regarding diabetes mellitus and smoking, we could not identify any discernible differences between the two groups (p= 0.332, p=1.0, respectively).

**Table (1):** Participants' demographic details.

| | Cases | Controls | Total | p value |
|---|---|---|---|---|
| Sex: | | | | |
| Male, n | 46 | 46 | 92 | |
| Female, n | 37 | 37 | 74 | |
| Age: | | | | |
| Mean ± SD | 65.93 ± 12.43 | 65.93 ± 12.43 | 65.93 ± 12.43 | |
| < 65 years, n | 35 | 35 | 70 | |
| ≥ 65 years, n | 48 | 48 | 96 | |
| Hypertension: | | | | |
| Yes, n | 71 | 39 | 110 | < 0.001 |
| No, n | 12 | 44 | 56 | |
| Diabetes mellitus: | | | | |
| Yes, n | 33 | 27 | 60 | 0.332 |
| No, n | 50 | 56 | 106 | |
| Smoking: | | | | |
| Yes, n | 12 | 12 | 24 | 1.0 |
| No, n | 71 | 71 | 142 | |
| Family history of stroke: | | | | |
| Yes, n | 23 | 9 | 32 | 0.01 |
| No, n | 57 | 67 | 124 | |
| Unknown, n | 3 | 7 | 10 | |
| Total, n | 83 | 83 | 166 | |

The chi-square test was used. n: number. SD: standard deviation.


https://doi.org/10.56056/amj.2026.450

We compared the mean serum zinc levels of the cases and the controls Table (2) and Figure (1). Although the mean zinc level of the cases was slightly less than that of the controls, the difference was not statistically significant (49.87 ± 13.43 µg/dL vs 52.61 ± 19.86 µg/dL, p=0.33). We found that 79 out of 83 cases (95.2%) had serum zinc levels below the normal range (70-115 µg/dL). On the other hand, 71 controls (85.5%) had low zinc levels and that difference was statistically significant (p=0.04).

**Table (2):** Comparison of the serum zinc levels of the cases and controls.

| | | Cases | Controls | Total | p value |
|---|---|---|---|---|---|
| Zinc | Mean ± SD (µg/dL) | 49.87 ± 13.43 | 52.61 ± 19.86 | 51.24 ± 16.43 | 0.33 |
| | Low (< 70 µg/dL), n (%) | 79 (95.2%) | 71 (85.5%) | 148 (89.2%) | 0.04 |
| | Normal (≥ 70 µg/dL), n (%) | 4 (4.8%) | 12 (14.5%) | 16 (9.6%) | |
| Total | | 83 (100%) | 83 (100%) | 166 (100%) | |

The independent t-test was utilized to compare continuous variables. The comparison of categorical variables was conducted using chi-square test. SD: standard deviation. n: number. %: percentage. We used the NIHSS to assess the severity of stroke in the cases. The NIHSS and the serum zinc levels had a negative relationship (r= -0.462, p<0.001). Depending on the NIHSS, we classified the severity of stroke as minor (1-4), moderate (5-15), moderate to severe (16-20), and severe (21-42). We found that 18 patients had minor, 39 had moderate, 14 had moderate to severe, and 12 had severe strokes Table (3). Significantly lower zinc levels were seen in patients with more severe strokes when we compared the mean serum zinc levels of these four groups (p=0.007), Figure (2).

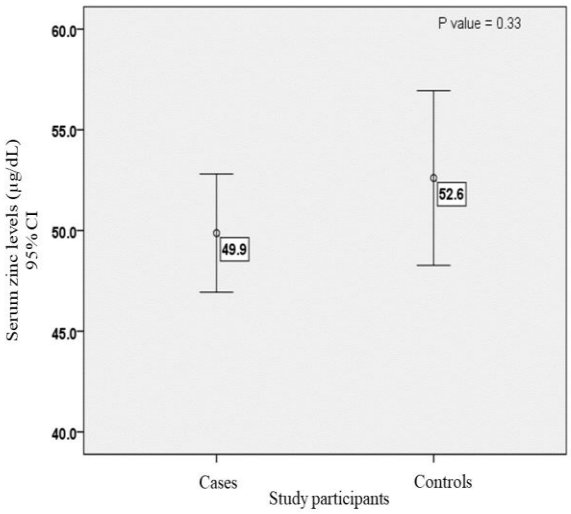


**Figure (1):** Mean serum zinc levels of the cases and the controls. CI: confidence interval.

**Table (3):** Serum zinc levels and severity of stroke.

| | Frequency | | Zinc level (µg/dL) | | p value |
|---|---|---|---|---|---|
| | | | Mean | Standard deviation | |
| NIHSS | Minor (1-4) | 18 | 56.40 | 7.17 | 0.007 |
| | Moderate (5-15) | 39 | 50.72 | 13.92 | |
| | Moderate to Severe (16-20) | 14 | 47.73 | 14.35 | |
| | Severe (21-42) | 12 | 39.83 | 12.85 | |
| Total | 83 | | 49.87 | 13.43 | |

ANOVA was used.


https://doi.org/10.56056/amj.2026.450

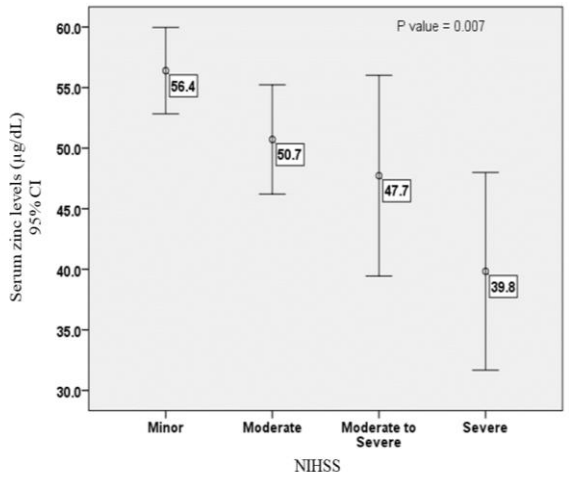


**Figure (2):** Mean serum zinc levels of stroke patients grouped with respect to severity of stroke. CI: confidence interval.

When attempting to find an association between the zinc levels of the stroke patients and their demographic characteristics, we found that male patients had significantly lower zinc levels (47.26 ± 12.93 µg/dL) compared to the female patients (53.12 ± 13.51 µg/dL) (p=0.047). Additionally, we discovered that age and serum zinc levels had a negative relationship (r= -0.258, p=0.02). Patients aged 65 years and over had significantly lower zinc levels (46.89 ± 14.26 µg/dL) than patients under 65 (53.96 ± 11.15 µg/dL) (p=0.02). As already mentioned, zinc levels were shown to be negatively correlated with each of NIHSS and age, but there was no correlation between NIHSS and age of the cases (r=0.176, p=0.11). Moreover, no relationship was found between the zinc levels of the cases and their other characteristics (hypertension, diabetes mellitus, smoking, family history of stroke). We tried to find a relationship between the zinc levels of the controls and their demographic characteristics, but there was no significant association. When we grouped the cases and the controls according to their characteristics and compared the mean zinc levels of the different groups with each other, we did not find any statistically significant difference except that the mean zinc level of the cases with a family history of stroke was significantly higher (52.62 ± 12.92 µg/dL) than that of the controls with a family history of stroke (40.81 ± 13.70 µg/dL) (p=0.03). Finally, comparing the mean zinc levels of the cases who received thrombolytic therapy (53.73 ± 14.35 µg/dL) and those treated conservatively (49.22 ± 13.27 µg/dL), no significant difference was seen (p=0.29).

## Discussion

Oxidative stress and inflammation play crucial roles in the development and progression of cardiovascular diseases.[12] Zinc has antioxidant and anti-inflammatory properties. Therefore, it has long been thought that zinc deficiency increases the risk of atherosclerosis and eventual cardiovascular disease. Yang et al. discovered that in adults without clinical cardiovascular disease, the average carotid intima-media thickness was greater in individuals with a low dietary zinc intake than in those with a high zinc intake when using the common carotid intima-media thickness as an indicator of subclinical atherosclerosis.[13] According to a meta-analysis, the serum and hair zinc levels of myocardial infarction patients were lower than those of healthy controls.[14] Preclinical studies examining the function of zinc in cerebral ischemia could not conclude whether zinc was neuroprotective, neurotoxic, or both.[3] Low serum zinc levels have been linked to ischemic stroke in some studies.[4,7–9] Most of these studies were case-control studies. Therefore, a causal relationship could not be established. A pre-existing deficiency may not always be the cause of low serum zinc levels in ischemic stroke patients; low zinc levels could be due to mobilization of circulating zinc into the ischemic brain tissue for antioxidant defense.[7] Alkanli et al., in contrast,


https://doi.org/10.56056/amj.2026.450

discovered that ischemic stroke patients had higher serum zinc levels than controls.[15] We assessed the zinc levels in the serum of 83 acute ischemic stroke patients and 83 control subjects. The mean serum zinc levels of the two groups did not differ statistically significantly, despite the fact that the majority of stroke patients had low blood zinc levels. Similarly, the mean zinc levels of 1277 cases and 1277 controls did not differ statistically significantly, according to Wen et al.[16] Furthermore, Zhang and colleagues did not find a significant link between plasma zinc levels and the likelihood of experiencing the first ischemic stroke in individuals with hypertension.[17] A prominent difference between our study and the previous studies that we reviewed is that the mean zinc levels of both the cases and the controls of our study were below the normal range and the majority of both groups had low zinc levels. However, our results were similar to those of a case-control study investigating serum zinc levels in pregnant women with anemia in Duhok, Kurdistan region, Iraq.[18] That study also indicated that the majority of the subjects in both the case group and the control group had low levels of zinc in their serum, with their average zinc levels falling below the normal range. Roughly 31% of people worldwide are thought to be zinc deficient.[5] A study measured serum zinc levels in a sample of 332 healthy participants in Duhok and found that 10% had zinc deficiency.[19] In contrast, another study recruiting 254 healthy smoker and non-smoker men in the same city showed that 45.4% of the participants had zinc deficiency.[20] Al-Timimi et al. found that 57.4% of 2090 healthy participants of all age groups had deficiency of zinc in Baghdad, Iraq.[21] We think two factors may have contributed to the apparent discrepancy in the results of serum zinc between some of the studies we cited in this paper. First, it is known that serum zinc levels can decrease when an inflammation is present.[22] Second, contamination from laboratory equipment, such as blood collection tubes, may falsely elevate serum zinc levels.[23,24] Royal blue-top tubes (dark blue-top tubes) are currently recommended for blood collection because they are free of metals. Zinc levels and stroke severity were found to be negatively correlated in our study, with lower serum zinc levels being linked to more severe strokes. The results of Bhatt et al., Mirończuk et al., and Kumar et al. are in line with this.[3,9,10] However, Suleiman et al. did not find such a correlation.[8] In our research, we also found that there is an inverse relationship between the age of stroke patients and their zinc levels, which aligns with the findings of Kumar et al.[10] Male patients with acute ischemic stroke were found to have significantly lower levels of serum zinc compared to female patients in our study. This differs from the findings of Suleiman et al., Mirończuk et al., and Kumar et al., as their studies did not demonstrate a statistically significant disparity in the serum zinc levels between male and female patients.[8-10] Consistent with the conclusions of Kumar et al., our investigation did not identify any significant correlation between the zinc levels of the stroke patients and the presence of hypertension, diabetes mellitus, or smoking. The relationship between serum zinc and ischemic stroke remains unclear and elusive. More research is needed to clarify the function of zinc in ischemic stroke. Our study has several limitations. One limitation is the relatively small sample size we have. Another limitation of this study is that it did not recruit healthy participants for the control group, rather it recruited patients who presented with other diseases and had no history of stroke. The lack of data about the previous zinc levels of the participants was another limitation. Despite the limitations, our paper gives valuable insights about zinc in ischemic stroke.


https://doi.org/10.56056/amj.2026.450

## Conclusion

Most of the patients with acute ischemic stroke had low serum zinc levels. However, the cases did not have a significantly different mean zinc level compared to the controls. The severity of stroke and serum zinc levels were found to be significantly inversely correlated; lower serum zinc levels were linked to more severe strokes. Additionally, a significant inverse relationship between the age of stroke patients and their serum zinc levels was discovered.

## Acknowledgment

We would like to thank all the participants of our study and the laboratory staff of Shar Hospital for their help.

## Conflicts of interest

We do not have any conflicts of interest to declare.

## References

1. O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. The Lancet. 2010;376(9735):112–23. doi:10.1016/S0140-6736(10)60834-3/
2. Marsh JD, Keyrouz SG. Stroke prevention and treatment. J Am Coll Cardiol. 2010 Aug 24;56(9):683–91. doi: 10.1016/j.jacc.2009.12.072/
3. Bhatt A, Farooq MU, Enduri S, Pillainayagam C, Naravetla B, Razak A, et al. Clinical significance of serum zinc levels in cerebral ischemia. Stroke Res Treat. 2010;2010. doi:10.4061/2010/245715/
4. Mattern L, Chen C, McClure LA, Brockman J, Cushman M, Judd S, et al. Serum zinc levels and incidence of ischemic stroke: the reasons for geographic and racial differences in stroke study. Stroke. 2021 Dec 1;52(12):3953–60. doi:10.1161/STROKEAHA.120.033187/
5. Caulfield L, Black R. Zinc deficiency. In: Ezzati M, Lopez A, Rodgers A, Murray CJL, editors. Comparative Quantification of Health Risks: Global and Regional Burden of Disease Attributable to Selected Major Risk Factors. Geneva: World Health Organization; 2004: 257–79.
6. Yanagisawa H. Zinc deficiency and clinical practice —Validity of zinc preparations—. Yakugaku Zasshi. 2008;128(3):333–9. doi:10.1248/YAKUSHI.128.333/
7. Munshi A, Babu S, Kaul S, Shafi G, Rajeshwar K, Alladi S, et al. Depletion of serum zinc in ischemic stroke patients. Methods Find Exp Clin Pharmacol. 2010;32(6):433–6. doi:10.1358/mf.2010.32.6.1487084/
8. Suleiman H, Aliyu I, Abubakar S, Anaja P, El-Bashir JM, Adamu R, et al. Assessment of homocysteine, vitamin B12, and zinc levels among patients with acute ischemic stroke in northwestern Nigeria. Niger J Basic Clin Sci. 2017;14(2):105–8. doi: 10.4103/njbcs.njbcs_49_16/
9. Mirończuk A, Kapica-Topczewska K, Socha K, Soroczyńska J, Jamiołkowski J, Kułakowska A, et al. Selenium, copper, zinc concentrations and Cu/Zn, Cu/Se molar ratios in the serum of patients with acute ischemic stroke in northeastern Poland—a new insight into stroke pathophysiology. Nutrients. 2021 Jul 1;13(7):2139. doi:10.3390/nu13072139/
10. Kumar A, Kubota Y, Chernov M, Kasuya H. Zinc deficiency may contribute to the severity of acute stroke in elderly patients: results of preliminary study and literature review. Tokyo Women's Med. Univ. j. 2021 Dec 20; 5:64–71. doi:10.24488/twmuj.2020013/
11. Beattie JH, Kwun IS. Is zinc deficiency a risk factor for atherosclerosis? Br J Nutr. 2004 Feb;91(2):177–81. doi:10.1079/bjn20031072/

12. Choi S, Liu X, Pan Z. Zinc deficiency and cellular oxidative stress: prognostic implications in cardiovascular diseases. Acta Pharmacol Sin. 2018 Jun 21;39(7):1120–32. doi:10.1038/aps.2018.25/
13. Yang YJ, Choi BY, Chun BY, Kweon SS, Lee YH, Park PS, et al. Dietary zinc intake is inversely related to subclinical atherosclerosis measured by carotid intima-media thickness. Br J Nutr. 2010 Oct 28;104(8):1202–11. doi:10.1017/S0007114510001893/
14. Liu B, Cai ZQ, Zhou YM. Deficient zinc levels and myocardial infarction. Biol Trace Elem Res. 2015 May 1;165(1):41–50. doi:10.1007/S12011-015-0244-4/
15. Alkanli N, Ay A, Kehaya S. Investigation of the relationship between ischemic stroke disease and serum zinc levels. Erciyes Med J. 2022;44(2):194–9. doi:10.14744/etd.2021.35589/
16. Wen Y, Huang S, Zhang Y, Zhang H, Zhou L, Li D, et al. Associations of multiple plasma metals with the risk of ischemic stroke: a case-control study. Environ Int. 2019 Apr 1; 125:125–34. doi: 10.1016/j.envint.2018.12.037/
17. Zhang J, Cao J, Zhang Y, Li H, Zhang H, Huo Y, et al. Baseline plasma zinc and risk of first stroke in hypertensive patients: a nested case-control study. Stroke. 2019 Jan 8;50(11):3255–8. doi:10.1161/STROKEAHA.119.027003/
18. Rasool SO, Zaman BA, Abdulah DM. Serum zinc levels in iron deficiency anemia, non-iron deficiency anemia, and normal pregnant women and its correlation with iron status and hematological parameters. Med J Babylon. 2020 Jan 1;17(1):103–8. doi: 10.4103/MJBL.MJBL_91_19/
19. Mahmoud HM, Al-Timimi DJ. Current zinc status among a healthy population in Duhok city, Iraq. Duhok Med J. 2012;6(1):70–6.
20. Al-Timimi DJ, Haji MR, Mohammad BY. Zinc status among smokers and non-smokers: relation to oxidative stress. Duhok Med J. 2010;4(1):67–73.
21. Al-Timimi DJ, Al-Sharbatti SS, Al-Najjar F. Zinc deficiency among a healthy population in Baghdad, Iraq. Saudi Med J. 2005 Nov 1;26(11):1777–81.
22. Galloway P, Mcmillan DC, Sattar N. Effect of the inflammatory response on trace element and vitamin status. Ann Clin Biochem. 2000 May 1;37(3):289–97. doi:10.1258/0004563001899429/
23. Mayo Foundation for Medical Education and Research. Metals analysis - collection and transport [Internet]. Mayo Clinic Laboratories. [cited 2024 Apr 5]. Available from: https://www.mayocliniclabs.com/test-notifications/attachment.phpid=1103/
24. Beresford P. Falsely elevated zinc results due to contamination of serum blood tubes [Internet]. North Bristol NHS Trust. 2020 [cited 2023 Jun 5]. Available from: https://www.nbt.nhs.uk/sites/default/files/document/Falsely%20elevated%20zinc%20results%20letter%2015th%20Oct%202020_0.pdf/