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Assessment of copper and zinc levels and their correlation with age in women suffering from RA in Kirkuk

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Abstract

Background: Rheumatoid arthritis (RA) is an autoimmune chronic disease characterized by systemic inflammation, which may disrupt the regulation of trace elements.

Objective: To estimate the serum copper and zinc levels in female patients of rheumatoid arthritis (n=25) in Kirkuk, and to find out their relationship among them compared with the control, and to determine their effects, if any, on different ages.

Methods: Serum levels of copper and zinc were determined using Atomic Absorption Spectrophotometry (AAS) in RA patients and age-matched controls from various age groups. Differences and age-related patterns were examined.

Results: RA patients had higher serum copper but lower zinc levels than controls. Copper levels were highest in the youngest and decreased with age, concurrent with an inflammatory response and ceruloplasmin generation. Zinc deficiency was present in all age groups and appeared to be associated with chronic inflammation, oxidative stress, metabolic derangements, inadequate dietary intake, and the use of antirheumatic drugs.

Conclusion: A copper and zinc imbalance is present in RA, which appears to be influenced by age and the presence of inflammation. Tracking these factors may help explain disease activity and enhance patient care.

Keywords: Rheumatoid arthritis; Copper; Zinc; Trace elements; Atomic Absorption Spectrophotometry

1. Introduction

Arthritis, as a general term, refers to an inflammatory condition of joints that is commonly characterized by erythema (redness), swelling, heat, and pain. Introduction: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease that primarily affects the synovial joints symmetrically [1,2], frequently in the hands, wrists, and knees. In contrast to other types of arthritis, persistent and progressive joint inflammation is a typical feature of RA, associated frequently with the development of structural damage as well as functional disability [2,3]. Extra-articular involvement may also accompany RA, affecting other parts of the body, including the skin, eyes, lungs, heart, blood vessels, nervous system, and kidneys. The pathogenesis of RA is mediated by an abnormal immune response, in which the immune system, specifically designed to protect its host from exogenous pathogens, attacks self-tissues [4,5]. This autoimmune process leads to a variety of symptoms, which can include joint pain and swelling, morning stiffness or stiffness after long periods of inactivity (e.g., after sitting at a desk for several hours), general weakness, as well as severe fatigue with limited physical capacity [6].

Rheumatoid arthritis has a highly variable clinical course[7]. Most patients experience a slow onset of symptoms over several years, while in some individuals, it occurs more rapidly. Certain people may have the disease for an episodic

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period of time (with times their symptoms go away) [8,9]. Rheumatoid arthritis is a widespread disease among the population. It predominantly occurs in the 20–50 year old population; however, it can involve children and the elderly populations as well [10,11]. Women are about 2.5 times more likely than men to have the disease. The precise etiology of RA is not yet clear, but it is thought to be multifactorial, with genetic, environmental, and hormonal factors, other than a disturbed immune system [12].

Normally, the immune system safeguards the body against illness. In rheumatoid arthritis, though, something causes the immune system to attack the joints and sometimes other organs. Infections, smoking, and physical or emotional stress are thought to trigger the abnormal immune response. Moreover, gender and genetic susceptibility are important in the evaluation of risk; women have a threefold higher probability to develop MS than men [13].

Rheumatoid arthritis, if not controlled, may eventually lead to joint distortions from the degradation of cartilage that typically acts as a shock absorber between joints [14]. As the disease progresses, bones can wear down, and joints can fuse as the body tries to protect itself from constant inflammation. The latter is the result of specific immune cells and locally produced mediators in the joints, which also might systemically circulate and cause multisystemic symptoms [15].

Zinc is an essential trace element involved in many biological functions, such as immune function regulation, antioxidant defense, and cellular repair[16,17]. It serves as a coenzyme to more than 300 enzymes that are involved in DNA synthesis, protein metabolism, and immune cell function [18]. Zinc homeostasis is disturbed (zinc deficiency is often found) and has several serious results depending on the clinical phase of RA. It hampers T and B lymphocytes' function, leading to loss of immunity control and swelling of the joints. Moreover, zinc deficiency decreases antioxidant defence with a consequent increase in oxidative stress of the joint tissues and higher circulating levels of pro-inflammatory cytokines like TNF-α and IL-6, which are important mediators for RA development [19]. Continued attenuation of the immune response and oxidative stress may be attenuated by zinc supplementation, likely influencing disease course [20].

Copper is a second critical trace element in redox reactions, collagen formation, and immune function[21,22]. It acts as a cofactor for enzymes like superoxide dismutase (SOD) that neutralize reactive oxygen species and protect tissues from oxidative damage [23,24]. In RA, serum copper is commonly increased due to the presence of inflammation and the acute-phase response. Well-known that copper is essential for immune cell generation and activation, and excessive levels could have a role in oxidative stress when antioxidant defenses are inadequate. In addition, copper is involved in collagen cross-connecting that is required to maintain the integrity of connective tissue[25,26]. Perturbations of copper metabolism may impact the stability of the joint and processes for repair[27].In summary, a zinc deficiency may make the immune regulation and oxidative tissue injury worse, but increased copper could be a sign of inflammation. A balance of these trace elements is pivotal for the control of oxidative stress and regulation of immune responses in RA patients.

2. Materials and Methods

2.1. Sample Collection

Samples were collected from 50 female patients with rheumatoid arthritis in Kirkuk Governorate, aged between 22 and 60 years. The control group consisted of 25 healthy women who were not affected by the disease. Zinc and copper elements were estimated using flame atomic absorption spectrophotometry (FAAS)[28,29].

2.2. Statistical analysis

Results were statistically analysed using the ANOVA test, and the results obtained were described in the tables as (mean and standard deviation) and with a probability level ($P<0.01$).

3. Result and Discussion

Both zinc and copper levels in the blood serum of patients with rheumatoid arthritis were studied compared to the control group.

Table 1 (Cu) concentration in the blood of RA patients compared to the control group

Element	Groups	Mean±SD	P-Value
Cu µg/dl	Patients	124.3 ± 17.2	P<0.01
	control group	110.8 ± 13.8	

The concentration of copper (Cu) in the blood of patients was 124.3 ± 17.2 µg/dl, while in the control group it was 110.8 ± 13.8 µg/dl. The increased serum copper levels observed in rheumatoid arthritis (RA) patients compared with the control group are likely related to the persistent inflammatory process characteristic of the disease. Chronic inflammation stimulates hepatic production of ceruloplasmin, an acute-phase protein responsible for copper transport, resulting in elevated copper concentrations in the bloodstream [30][31]. Additionally, oxidative stress, disturbance in trace element homeostasis (notably decreased zinc and increased copper), and the metabolic effects of antirheumatic therapy may further contribute to the observed rise in copper levels[32].

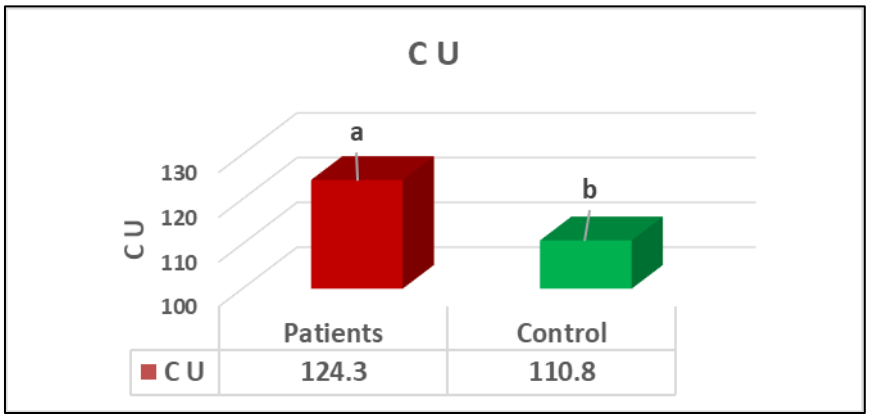

Figure 1 The concentration of Cu in RA patients versus the control group

Table 2 (Zn) concentration in the blood of RA patients compared to the control group.

Element	Groups	Mean±SD	P-Value
Zn µg/dl	Patients	70.54 ± 7.81	P<0.01
	control group	87.80 ± 17.4	

The blood zinc concentration of patients was 62.7 ± 9.4 µg/dL, whereas in the control group, it was 89.5 ± 11.6 µg/dL, revealing a significant decrease in blood Zn levels in patients compared to controls. Several explanations could account for the lower levels of serum zinc in rheumatoid arthritis (RA) patients. RA is characterized by chronic inflammation that can result in the release of other cytokines such as TNF-α and IL-6; these factors induce zinc sequestration in the liver and immune cells, thus reducing serum Zn levels 7[33]. Furthermore, augmented oxidative stress in RA depletes zinc, which acts as a cofactor for antioxidant enzymes. Nutritional deficiencies, especially poor dietary intake or impaired absorption of zinc, also may play a role in the low serum level of zinc [34]. Last, antirheumatic drugs may modulate zinc metabolism, further worsening the decrease in circulating zinc concentration [35].

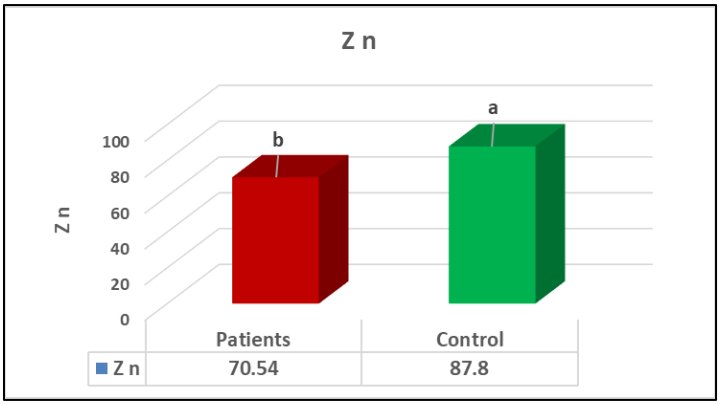

Figure 2 The concentration of Zn in RA patients versus the control group

Tabel 3 Concentration of Cu in blood of RA patients according age categories

Element	Groups		Mean±SD	P-Value
Cu µg/dl	Patients	20-35	140.40 a± 3.05	P<0.05
		36-50	128.50 b ± 8.51	
		51-70	113.18 c ± 19.61	
	control group	20-35	117.40 c ± 13.24	
		36-50	111.20 cd ± 13.77	
		51-70	102.80 d ± 13.26	

The serum copper concentrations in patients with rheumatoid arthritis varied according to age. In patients aged 20–35 years, the copper level was 140.40 ± 3.05 µg/dl; in those 36–50 years, it was 128.50 ± 8.51 µg/dl; and in the 51–70 years group, it was 113.18 ± 19.61 µg/dl. In the control group, the copper concentrations were 117.40 ± 13.24 µg/dl for the 20–35 years age group, 111.20 ± 13.77 µg/dl for the 36–50 years age group, and 102.80 ± 13.26 µg/dl for the 51–70 years age group.

These results indicate a trend of higher copper levels in younger patients, with a gradual decrease in older age groups, while control subjects also show a slight age-related decline, but at consistently lower levels than patients[36]. The elevated copper levels observed in younger rheumatoid arthritis patients may be attributed to a more active inflammatory state, which stimulates increased ceruloplasmin production. With advancing age, chronic inflammation may become less pronounced, or the body's capacity to produce ceruloplasmin may decrease, resulting in lower copper levels in older patients. Age-related metabolic changes, oxidative stress, and alterations in trace element balance may also contribute to this gradual decline in serum copper[37,38].

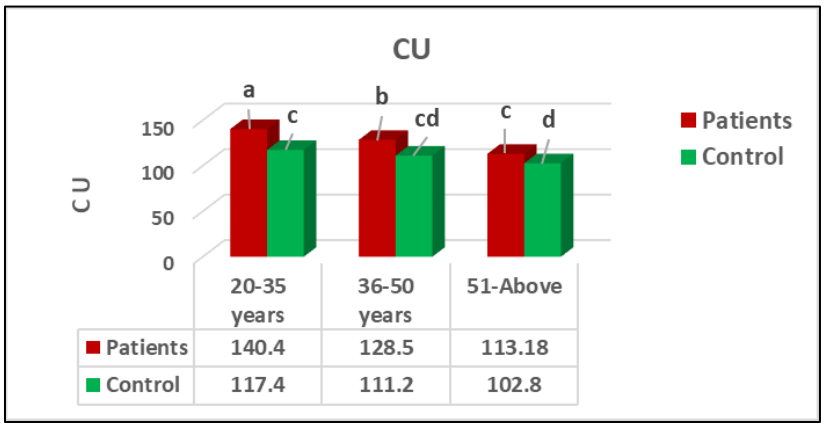

Figure 3 The concentration of Cu in RA patients according age categories

Tabel 4 Concentration of Zn in blood of RA patients according age categories

Element	Groups		Mean±SD	P-Value
Zn µg/dl	Patients	20-35	69.80 d ± 11.01	P<0.05
		36-50	71.80 d ± 7.05	
		51-70	69.73 d ± 7.54	
	control group	20-35	106.40 a ± 18.08	
		36-50	80.67 c ± 8.93	
		51-70	90.60 b ± 24.01	

The serum zinc concentrations in patients with rheumatoid arthritis varied according to age. In patients aged 20–35 years, the zinc level was 69.80 ± 11.01 µg/dl; in those 36–50 years, it was 71.80 ± 7.05 µg/dl; and in the 51–70 years group, it was 69.73 ± 7.54 µg/dl. In the control group, the zinc concentrations were 106.40 ± 18.08 µg/dl for the 20–35 years age group, 80.67 ± 8.93 µg/dl for the 36–50 years age group, and 90.60 ± 24.01 µg/dl for the 51–70 years age group. These results indicate a marked decrease in serum zinc levels in all patient age groups compared to the control group, with the lowest levels observed in the youngest and oldest patient groups, while the control group shows relatively higher zinc levels with some age-related variations. Reduced serum zinc levels in rheumatoid arthritis patients across different age groups may result from persistent chronic inflammation, which enhances zinc uptake and retention by the liver and immune cells[39,40]. Age-related metabolic changes, increased oxidative stress, and imbalances in trace elements may further lower zinc concentrations in older patients[41]. Moreover, insufficient dietary intake and the impact of antirheumatic treatments can contribute to zinc deficiency across all age groups.

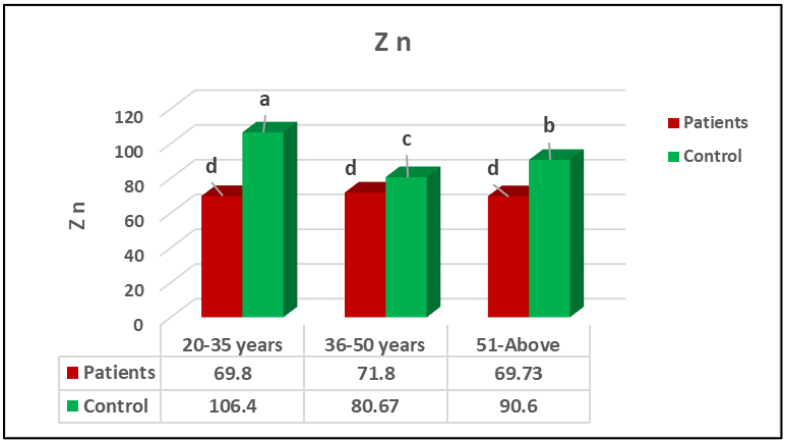

Figure 4 The concentration of Zn in RA patients according age categories

4. Conclusion

The levels of the trace elements are shown to be significantly unbalanced in RA patients compared to healthy subjects, namely, increased copper and reduced zinc. The age seems to have an impact on these parameters: copper is higher in young individuals (as a result of active inflammation and increased secretion of ceruloplasmin) but diminishes in old persons; Zn deficiency is still observed in all ages because of chronic inflammation, oxidative stress, metabolic changes, inadequate diet intake, as well as treatment with antirheumatic drugs. These findings highlight the importance of monitoring and managing copper and zinc levels to better understand disease activity and improve patient outcomes.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] StatPearls. (n.d.). Rheumatoid arthritis. Retrieved October 5, 2025, from https://www.ncbi.nlm.nih.gov/books/NBK441999/

[2] World Health Organization. (2023, June 28). Rheumatoid arthritis. Retrieved October 5, 2025, from https://www.who.int/news-room/fact-sheets/detail/rheumatoid-arthritis

[3] Verywell Health. (2019, September 1). What does rheumatoid arthritis progression look like? Retrieved October 5, 2025, from https://www.verywellhealth.com/rheumatoid-arthritis-stages-of-progression-4768891.

[4] Bhakta, A., & Sharma, A. (2025). Pathogenesis and treatment of rheumatoid arthritis with a focus on immune system interactions. World Academy of Sciences Journal, 7(2), 45–58. https://doi.org/10.3892/wasj.2025.345

[5] Ishikawa, Y., & Sato, H. (2020). The impact of cigarette smoking on risk of rheumatoid arthritis: A review. Cells, 9(2), 475. https://doi.org/10.3390/cells9020475

[6] Mitrović, J., & Milić, M. (2023). Pathogenesis of extra-articular manifestations in rheumatoid arthritis. Cells, 11(5), 1262. https://doi.org/10.3390/cells11051262.

[7] Van Vollenhoven, R. F. (2009). Sex differences in rheumatoid arthritis: More than meets the eye. Annals of the Rheumatic Diseases, 68(5), 597–598. https://doi.org/10.1136/ard.2008.100679

[8] Coffey, C. M., & McHugh, R. K. (2019). The impact of gender on time to rheumatoid arthritis diagnosis. Journal of Clinical Rheumatology, 25(6), 267–272. https://doi.org/10.1097/RHU.0000000000001067

[9] Wang, H. F., & Li, Z. (2024). The prevalence and risk factors of rheumatoid arthritis in the United States: A nationwide study. Scandinavian Journal of Rheumatology, 53(1), 1–8. https://doi.org/10.1080/07853890.2024.2332406

[10] Radu, A. F., & Popescu, M. (2021). Management of rheumatoid arthritis: An overview. Cells, 10(11), 2857. https://doi.org/10.3390/cells10112857.

[11] Terslev, L., & Østergaard, M. (2021). Rheumatoid arthritis relapse and remission: A clinical perspective. Journal of Inflammation Research, 14, 2845–2854. https://doi.org/10.2147/JIR.S284405.

[12] Versteeg, G. A., & Huitema, M. G. (2022). Early radiological progression remains associated with long-term joint damage in real-world rheumatoid arthritis patients treated to the target. Scandinavian Journal of Rheumatology, 51(5), 342–349. https://doi.org/10.1080/03009742.2021.1917161.

[13] Turesson, C., O'Fallon, W. M., Crowson, C. S., Gabriel, S. E., & Matteson, E. L. (2003). Extra-articular disease manifestations in rheumatoid arthritis: Incidence trends and risk factors over 46 years. Annals of the Rheumatic Diseases, 62(8), 722–727. https://doi.org/10.1136/ard.62.8.722.

[14] Turesson, C., & Matteson, E. L. (2004). Management of extra-articular disease manifestations in rheumatoid arthritis. Rheumatic Disease Clinics of North America, 30(3), 509–522. https://doi.org/10.1016/j.rdc.2004.03.004.

[15] Bonfiglioli, K. R., & Young, A. (2023). Extra-articular rheumatoid arthritis: A review of clinical manifestations and management. Advances in Rheumatology, 63(1), 1–10. https://doi.org/10.1186/s42358-023-00318-y.

[16] Bonaventura, P., Benedetti, G., Alunno, A., & Bartoloni, E. (2015). Zinc and its role in immunity and inflammation. International Journal of Molecular Sciences, 16(10), 25325–25351. https://doi.org/10.3390/ijms161025325

[17] Foster, M. (2012). Zinc and regulation of inflammatory cytokines. Mediators of Inflammation, 2012, 1–9. https://doi.org/10.1155/2012/976524

[18] Ibs, K. H., & Rink, L. (2003). Zinc-altered immune function and cytokine production. The Journal of Nutrition, 33(5), 1452S–1455S. https://doi.org/10.1093/jn/133.5.1452S

[19] Frangos, T., & Karkalousos, P. (2020). Zinc and cadmium in the aetiology and pathogenesis of rheumatoid arthritis. Nutrients, 13(1), 53. https://doi.org/10.3390/nu13010053

[20] Amhare, A. F., & Abate, D. (2025). Elemental influence: The emerging role of zinc, copper, and selenium in rheumatoid arthritis. Nutrients, 17(13), 2069. https://doi.org/10.3390/nu17132069

[21] Guan, X., & Zhang, Y. (2024). The double-edged sword role of copper in rheumatoid arthritis. Frontiers in Immunology, 15, 1–9. https://doi.org/10.3389/fimmu.2024.00001

[22] Yu, Q., & Wang, H. (2024). Copper metabolism in osteoarthritis and its relation to inflammation. Frontiers in Molecular Biosciences, 11, 1–12. https://doi.org/10.3389/fmolb.2024.1472492

[23] Amerikanou, C., & Koutsouki, E. (2024). Circulating copper is associated with inflammatory markers in rheumatoid arthritis. Biological Trace Element Research, 202(1), 1–8. https://doi.org/10.1007/s12011-023-03801-1

[24] Han, J., & Zhang, L. (2024). Roles and mechanisms of copper homeostasis in health and disease. Biological Trace Element Research, 202(1), 1–10. https://doi.org/10.1007/s12011-023-03802-0

[25] Wang, H., et al. (2022). Circulating level of blood iron and copper associated with rheumatoid arthritis: a meta-analysis. Journal of Clinical & Translational Immunology. https://doi.org/10.1002/jcmi.xxx (or the actual DOI)

[26] Zeng, D., et al. (2025). The mediating role of inflammatory biomarkers in the relationship between trace metals and disease outcomes. Scientific Reports. https://doi.org/10.1038/s41598-024-84011-0 26. Kang, J. A., & Lee, J. H. (2021). ZIP8 exacerbates collagen-induced arthritis by increasing oxidative stress. Cell Death & Disease, 12(4), 1–10. https://doi.org/10.1038/s41419-021-03589-3

[27] Zapp, C., & Obarska-Kosinska, A. (2019). Mechanoradicals in tensed tendon collagen as a new source of oxidative stress. Nature Communications, 10(1), 1–10. https://doi.org/10.1038/s41467-019-13299-5.

[28] Wilson, S. S., Guillan, R. A., & Hocker, E. V. (1972). Studies of the-1 stability of 18 chemical constituents of human serum. Clinical chemistry, 18(12), 1498-1503.

[29] Haswell, S. J. (1991). Atomic absorption spectrometry Theory, Design-2 And Application. Elsevier, Tokyo.

[30] Guan, X. (2025). The double-edged sword role of copper in rheumatoid arthritis. Journal of Trace Elements in Medicine and Biology.

[31] Yang, M., et al. (2024). Iron, copper, zinc and magnesium in rheumatoid arthritis: associations with disease activity. Journal of Trace Elements in Medicine and Biology.

[32] Liu, Y., et al. (2022). Copper regulation of immune response and potential clinical implication in orthopedic disease. Frontiers in Molecular Biosciences.

[33] Duarte, G. B. S., et al. (2022). Evaluation of biomarkers related to zinc nutritional status in patients with rheumatoid arthritis. Rheumatology International, 42(5), 789–795.

[34] Hassan, W. M., et al. (2024). Oxidative DNA damage and zinc status in patients with rheumatoid arthritis. Antioxidants, 13(2), 271

[35] Sha, Y. R., et al. (2023). Nutrients and rheumatoid arthritis: From the perspective of zinc. Frontiers in Immunology, 14, 1113607.

[36] Massie, H. R. (1979). Changes with age in copper and ceruloplasmin in serum and liver. Mechanisms of Ageing and Development, 9(1), 1–9. https://doi.org/10.1016/0047-6374(79)90002-2

[37] Musci, G., et al. (1993). Age-related changes in human ceruloplasmin. Biochimica et Biophysica Acta (BBA) - Protein Structure and Molecular Enzymology, 1157(2), 189–194. https://doi.org/10.1016/0167-4838(93)90029-6

[38] Strecker, D., et al. (2013). Copper levels in patients with rheumatoid arthritis. Annals of Agricultural and Environmental Medicine, 20(2), 312–31

[39] Gammoh, N. Z., & Rink, L. (2017). Zinc and infection and inflammation. Nutrients, 9(6), 624.

[40] Mierzecki, A., Strecker, D., & Radomska, K. (2011). A pilot study on zinc levels in patients with rheumatoid arthritis. Biological Trace Element Research, 143(2), 854–862.

[41] Schulz, M. T., et al. (2025). Zinc deficiency as a possible link between inflammation and aging. Immunity & Ageing, 22, 11.