

ZINC AND MAGNESIUM VS COVID - 19

Barbara Sokołowska¹⁾, Stanisława Katarzyna Nazaruk¹⁾, Agnieszka Radzka-Pogoda²⁾, Gabriela Henrykowska³⁾, Andrzej Borzęcki⁴⁾

¹⁾ John Paul II University of Applied Sciences in Białą Podlaską, Poland

²⁾ Doctoral School, Medical University of Lublin, Poland

³⁾ Department of Epidemiology and Public Health, Medical University, Łódź, Poland

⁴⁾ Department of Hygiene and Epidemiology, Medical University of Lublin, Poland

ABSTRACT

Zinc and magnesium are among the most important elements for the human body. A deficiency or excess of either of them may pose a potential threat to the homeostatic mechanisms of the body. Both elements condition the proper functioning of the immune system. Zinc and magnesium deficiency significantly reduces the body's immunity, facilitating infection with various pathogens, including SARS-COV-2 infection. In this paper, we reviewed the literature on the impact of zinc and magnesium deficiencies on the incidence and course of COVID-19.

Keywords: zinc, magnesium, COVID-19, SARS-CoV2.

ARTICLE INFO

PolHypRes 2022 Vol. 79 Issue 2 pp. 45 – 52

ISSN: 1734-7009 **eISSN:** 2084-0535

DOI: 10.2478/phr-2022-0009

Pages: 8, figures: 5, tables: 0

page www of the periodical: www.phr.net.pl

Review article

Submission date: 24.01.2022 r.

Acceptance for print: 17.04.2022 r.

Publisher

Polish Hyperbaric Medicine and Technology Society



INTRODUCTION

Zinc and magnesium are both essential for the normal development, maturation and functioning of the human body. A deficiency or excess of either of these elements may pose a potential threat to the proper functioning of the homeostatic processes of the body [1,2].

Magnesium is a chemical element essential to all living organisms. It performs very important functions in the human body. It is an activator of over 300 enzyme reactions, catalysing reactions of the respiratory pathway, synthesis of nucleic acids, protein, fat and carbohydrate metabolism. It influences the permeability and stabilisation of cell membranes. The element is involved in the contraction of cardiac muscle cells and the regulation of blood pressure. Furthermore, it plays an

important role in bone mineralisation processes and calcium-phosphate metabolism, and regulates glycaemia. Magnesium is involved in the conduction of nerve impulses. It also influences the function of the immune system. 60% of magnesium is deposited in the human skeletal system and 20% in the skeletal muscles. The remaining amount of this element is distributed in other tissues and organs, such as the kidneys, liver and gastrointestinal tract. Only about 1% of magnesium is found in the extracellular space. The daily requirement for magnesium increases as the body grows, as well as during pregnancy, during intense physical and mental exertion, under stress and with alcohol abuse [3,4].

Table 1 shows the average daily magnesium demand for different age groups.

Tab. 1

Average daily magnesium requirements by age [5].

Magnesium requirements (mg/24h)					
Newborns and infants	Children at the age of 1-3 years	Children at the age of 4-9 years	Adolescents at the age of 10-12 years	Adolescents at the age of 13-18 years	Adults >18 years
30-70	65	110	200	300-340	265-350

The main cause of magnesium deficiency is a poorly balanced diet with a low magnesium content or a high content of ingredients that impede magnesium absorption. Other causes include impaired magnesium absorption in the course of pancreatitis, malabsorption syndrome and chronic use of proton pump inhibitors. Magnesium deficiency may also result from excessive magnesium loss (e.g. in chronic alcoholism, renal disease, primary hyperparathyroidism, vomiting and diarrhoea) [6]. Symptoms of magnesium deficiency are uncharacteristic. The most common symptoms are metabolic disorders such as hypocalcaemia, hypokalaemia and hypophosphataemia. They also include cardiac arrhythmias, neuromuscular symptoms including tremor in the arms, legs, tongue, lips, eyelids, painful muscle spasms, numbness, tingling in the limbs, weakness in muscle strength. Magnesium deficiency can lead to an increase in blood pressure and coronary heart problems associated with myocardial ischaemia. Symptoms such as chronic fatigue, difficulty in concentration and attention, impaired memory, excessive nervousness and irritability, and hair loss may also occur. A consequence of immune system dysfunction are frequent infections, mainly of the respiratory system, of varying aetiologies [7].

Zinc is another micronutrient with very important functions in the human body. The highest levels of this element are found in skeletal muscles and bones. Large amounts of zinc are also found in the liver, brain, prostate gland, skin and hair.

The element is a component of over 300 enzymes, including those that form the antioxidant barrier and those involved in the synthesis of proteins and nucleic acids. Zinc plays an important role in the processes of replication and transcription of genetic material and in gene expression and stabilisation processes. It participates in the processes of protein, fat and carbohydrate metabolism. It influences the synthesis

and function of steroid hormones. This element is essential in stabilising cell membranes, it conditions the proper functioning and regeneration of the skin and mucous membranes, and plays an important role in bone mineralisation processes. Zinc influences the immune system and participates in the body's immune reactions. Moreover, it is necessary for normal cell division, plays an important role in the body's ageing processes and in cell apoptosis. Zinc is also involved in blood clotting. Within the central nervous system, zinc influences learning and memory processes. It also plays an important role in the proper functioning of the senses of sight, hearing, smell and taste. It is also necessary for the proper functioning of the reproductive organs. Through participation in the biosynthesis and release of insulin, it is essential for the proper functioning of the pancreas. In addition, zinc is responsible for the metabolism of alcohol and reduces the toxic effects of heavy metals. Zinc is not produced or stored in the human body [8].

For this reason, it must be supplied with food in the daily diet. The absorption of zinc is inhibited by, inter alia, alcohol, fibre, oxalates and phytates. The main sources of zinc are animal products such as meat, eggs, fish and oysters, and, to a lesser extent, vegetable sources (sunflower seeds, pumpkin seeds, wheat germ and wheat bran, as well as garlic, onions). The daily zinc requirement depends on a number of factors, including, but not limited to, gender and age. The average daily zinc requirement for an adult is estimated to be approximately 15 mg. Table 2 shows the daily zinc requirement for different age groups [9].

Average daily zinc requirement by age [9].

Zinc requirements (mg/24h)						
Newborns and infants	Children at the age of 1-3 years	Children at the age of 4-9 years	Adolescents at the age of 10-12 years	Adolescents at the age of 13-18 years	Adults >18 years	
2.5	2.5	4	7	7.3-8.5	6.8-9.4	

Methods

A literature review from PubMed, Scopus, and Google Scholar databases was performed to assess the impact of magnesium and zinc deficiency on the incidence and course of COVID-19. Analysis of the data obtained may allow the development of scenarios for prevention and supplementation of magnesium and zinc in patients with SARS-CoV-2 infection. Key words searched included: magnesium, zinc, COVID-19, SARS-CoV2.

MAGNESIUM DEFICIENCY AND COVID-19

COVID-19 (coronavirus disease 2019) is a respiratory infectious disease caused by severe acute respiratory syndrome coronavirus2 (SARS-CoV-2) infection. The disease was first recognised and described in November 2019 in the city of Wuhan, Hubei province, central China. On 30 January 2020, a public health emergency of international concern was declared as a result of the spreading COVID-19 outbreak, and on 11 March 2020, a series of COVID-19 cases escalating since November 2019 was declared a pandemic by the World Health Organisation [10].

SARS-CoV-2 belongs to the group of coronaviruses with a single RNA strand and a corona-like envelope. The virus is highly infectious. It is transmitted by the droplet route. The main symptoms of COVID-19 typically include fever, cough, shortness of breath, fatigue, muscle aches, weakness, sore throat and general malaise. The clinical course of the disease varies from mild or even asymptomatic to severe respiratory failure and death [11]. The prognosis is worse in the elderly, in patients with comorbidities and immunocompromised patients. It has been shown that more than 80% of COVID-19 deaths were in people over 60 years of age, and more than 75% of those who died had comorbidities [11,12,13].

A well-balanced diet containing all the necessary micro- and macronutrients, a healthy lifestyle, and the ability to cope with stress have a significant impact on the human immune system [14,15]. The stress of social isolation during the COVID-19 pandemic and the fear of contracting the disease, the change in eating habits during lockdown, combined with reduced physical activity are the cause of a number of negative health implications, such as obesity, diabetes, cardiovascular diseases, which further weaken the human body's immune response to various pathogens, facilitating the development of infections and worsening their course and prognosis [16,17,18]. The authors Wolf FI. et al [19] demonstrated in their work the presence of magnesium deficiency in patients with said conditions. These authors also confirmed that hypomagnesaemia was an additional factor exacerbating the risk of COVID-19 and increasing

mortality in the course of this disease. Similar findings were obtained by researchers Alamdari NM. et al. [20], who showed that in patients hospitalised with COVID-19, magnesium deficiency influenced the lack of effect of the applied treatment and significantly increased the risk of death.

Further authors: Trapani V. et al. [4] concluded that magnesium acts as a cofactor for many enzymes, regulating ion channels and energy production, and is essential for maintaining normal physiology and cellular metabolism [21]. Magnesium deficiency increases the risk of inducing an inflammatory 'cytokine storm' and damaging the vascular endothelium as well as triggering the coagulation cascade. The consequence of these abnormalities is disseminated intravascular coagulation and the development of multi-organ failure [3,22]. Low magnesium levels induce the release of pro-inflammatory cytokines, promote platelet aggregation, release of beta-thromboglobulin and thromboxanes. Vascular endothelial damage and hypercoagulable state are key components of Virchow's triad and are responsible for the increased incidence of thromboembolic complications in patients with COVID-19 [21,23,24]. Magnesium deficiencies may also exacerbate the inflammatory response induced by SARS-CoV-2. Furthermore, other symptoms reported by patients with COVID-19, such as asthenia, myalgia, anxiety, depression, insomnia, may be related, not only to the viral infection, but also to magnesium deficiency [25]. The data from the literature review seem to confirm the link between impaired magnesium homeostasis and COVID-19 and motivate for further studies to investigate the preventive and therapeutic potential of magnesium supplementation.

ZINC DEFICIENCY AND COVID-19

Zinc occurs in the human body as a trace element. More than one third of the population suffer from its deficiency. Zinc plays a significant role in the normal functioning of the human immune system and in fighting infections [26,27]. The element has antiviral and immunomodulatory properties, and is a component of antioxidant enzymes that can inhibit virus reproduction in host cells and facilitate virus elimination. Low zinc levels cause immune system dysfunction and increase the risk of COVID-19 thus affecting the clinical course of the disease [28]. The results of studies by various authors indicate the existence of a correlation between the frequency of SARS-CoV-2 infection and zinc deficiency [28,29]. A significant correlation between serum zinc levels in COVID-19 patients and the severity of clinical manifestations of the disease and response to treatment has been confirmed. [30,31]. The work of Jothimani et al. [32] indicates the impact of zinc deficiency on the occurrence of severe complications and increased

mortality among patients hospitalised with COVID-19. Researchers Derwand R et al. and Im JH et al. [31,33] demonstrated that patients with severe COVID-19 symptoms had 8% lower serum zinc levels as compared to other patients. Furthermore, studies by Talha KA et al. [34] and by Shang W. et al. [35] showed a double incidence of the need for intensive oxygen support in zinc-deficient COVID-19 patients. Randomised studies by the authors: Patel et al. [36] showed that intravenous zinc supplementation reduced the severity of clinical symptoms in the acute phase of COVID-19. However, this was not confirmed by studies by other authors, indicating that the role of zinc in the prevention and treatment of COVID-19 is unclear [37, 38, 39].

In the course of COVID-19, intracellular zinc deficiency increases, which may affect the activity of carbonic anhydrase located in the taste buds and salivary glands. The consequence is an adverse effect on taste sensations and salivary secretion. Zinc supplementation reduces taste disorders and salivary gland dysfunction [40].

CONCLUSION

Content analysis of selected articles showed a correlation between magnesium and zinc deficiency and the risk of COVID-19, the clinical course of the disease and

prognosis. Supplementation of these elements may be helpful in preventing coronavirus infection and alleviating COVID-19 symptoms. The need exists to find effective treatments for COVID-19 and preventive measures to prevent SARS-CoV-2 infection. According to many experts, a healthy lifestyle, including appropriately dosed physical activity and a change in dietary habits, is of particular importance for the maintenance of normal system homeostasis. These factors reduce the risk of contracting COVID-19 and, in the event of illness, can significantly reduce the risk of complications of the disease. An individual assessment of possible dietary, nutritional, medical, lifestyle and environmental risks is necessary. Studies on the effects of magnesium and zinc on the possibility of infection and the course of COVID-19 need to be continued for setting specific prevention recommendations. To date, the most effective method of preventing infection remains vaccination.

REFERENCES

- Zhang E., He W., Du H., Yang K. (2008). Microstructure, mechanical properties and corrosion properties of Mg–Zn–Y alloys with low Zn content. *Materials Science and Engineering A* 488 (2008) 102–11. doi:10.1016/j.msea.2007.10.056;
- Human Vitamin and Mineral Requirements. Report of a joint FAO/WHO expert consultation Bangkok, Thailand. Food and Agriculture Organization of the United Nations. World Health Organization. Food and Nutrition Division FAO Rome.FAO 2001;
- Maier J. A., Pickering G., Giacomoni E., Cazzaniga A., Pellegrino P. (2020). Headaches and Magnesium: Mechanisms, Bioavailability, Therapeutic Efficacy and Potential Advantage of Magnesium Pidolate. *Nutriens*, 12(9):2660. doi: 10.3390/nu12092660;
- Trapani V., Rosanoff A., Baniyadi S., Barbagallo M., Castiglioni S., Guerrero-Romero F., Iotti S., Mazur A., Micke O., Pourdowlat G., Scarpati G., Wolf F.I., Maier J.A. (2022). The relevance of magnesium homeostasis in COVID-19. *European Journal of Nutrition*, volume 61(2):625-636. doi: 10.1007/s00394-021-02704-y;
- Razzaque M.S. Magnesium: Are We Consuming Enough? *Nutrients*. 2018; 10(12): 1863. doi: 10.3390/nu10121863;
- Medeiros de Moraes C. (2021). Nutritional therapy in COVID-19 management. *Kompass Nutr Diet*. 1:10-12. doi:10.1159/000512853;
- Coman AE., Ceasovschi A., Petroaie D.A., Popa E., Lionte C., Bologa C., Haliga R.E., Cosmescu A., Slănină A.M., Bacușcă A.I., Șorodoc V., Șorodoc L. (2023). The Significance of Low Magnesium Levels in COVID-19 Patients. *Medicina*, 59(2),279. doi: 10.3390/medicina59020279;
- Fan Y, Pedersen O. (2021). Gut microbiota in human metabolic health and disease. *Nat Rev Microbiol* 19:55–71. doi:10.1038/s41579-020-0433-9;
- Jarosz M., Rychlik E., Stoś K., Charzewska J. (red.) (2020) Nutrition standards for the Polish population and their application. Warszawa: Narodowy Instytut Zdrowia Publicznego – Państwowy Zakład Higieny. ISBN:978-83-65870-28-5;
- Hu B., Guo H., Zhou P., Shi, ZL. (2021). Characteristics of SARS-CoV-2 and COVID-19. *Nat. Rev. Microbiol.* 19, 141-154. doi:10.1038/s41579-020-00459-7;
- Ye Q, Wang B, Mao J., Fu J., Shang S., Shu Q., Zhang T. Epidemiological analysis of COVID-19 and practical experience from China. *J Med Virol* 2020; 92: 755-769;
- Harrison SL., Fazio-Eynullayeva E., Lane DA, Underhill P., Lip G.Y.H (2020). Comorbidities associated with mortality in 31,461 adults with COVID-19 in the United States: a federated electronic medical record analysis. *PLoS Med*, 17:1003321. doi:10.1371/journal.pmed.1003321;
- Salinas Aguirre JE., Sánchez García C., Rodríguez Sánchez R., Rodríguez-Sánchez R., Rodríguez-Muñoz L., Díaz-Castaño A., Bernal-Gómez R. (2021). Clinical characteristics and comorbidities associated with mortality in patients with COVID-19 in Coahuila (Mexico). *Rev Clin Esp*, 222(5): 288–292. doi: 10.1016/j.rceng.2020.12.007;
- Mikulec A., Zborowski M., Cisoń-Apanasewicz U., Stawiarska A., Kowalski S. (2022). Impact of the COVID-19 pandemic on the eating behaviour of children and adolescents. *Food. Science. Technology. Quality*, 29, 3 (132),42-55. doi:10.15193/zntj/2022/132/422;
- Galluccio A., Caparello G., Avolio E., Manes E., Ferraro S., Giordano C., Sisci D., Bonfiglio D. (2021). Self-perceived physical activity and adherence to the Mediterranean diet in healthy adolescents during COVID-19: findings from the DIMENU pilot study. *Healthcare*, 9(6), 622. doi: 10.3390/healthcare9060622;
- Khan M., Moverley-Smith JE. (2020). "Covibesity," a new pandemic. *Obes. Med.* 19,100282. doi: 10.1016/j.obmed.2020.100282;
- Dunn C.G., Kenney E., Fleischhacker S.E., Bleich S.N. (2020). Feeding low-income children during the covid-19 pandemic. *N. Engl. J. Med.* 382(18):e40. doi:10.1056/NEJMp2005638;
- Dunton G.F., Do B., Wang S.D. (2020). Early effects of the COVID-19 pandemic on physical activity and sedentary behavior in children living in the U.S. *BMC Public Health*. 4;20 (1): 1351. doi:10.1186/s12889-020-09429-3;
- Wolf FI., Maier JA., Rosanoff A., et al. (2021). The magnesium global network (MaGNet) to promote research on magnesium in diseases focusing on COVID-19. *Magnes Res*, 34:90–92. doi:10.1684/mrh.2021.0479;
- Alamdari N.M., Afaghi S., Rahimi F.S., Tarki F.E., Tavana S., Zali A., Fathi M., Besharat S., Bagheri L., Pourmotahari F., Irvani S.S.N., Dabbagh A., Mousavi S.A. Mortality Risk Factors among Hospitalized COVID-19 Patients in a Major Referral Center in Iran. *Tohoku J Exp Med*. 2020, 252(1), 73-84;
- Goshua G., Pine AB., Meizlish ML. et al. (2020). Endotheliopathy in COVID-19-associated coagulopathy: evidence from a single-centre, cross-sectional study. *Lancet Haematol*, 7:575-582. doi: 10.1016/S2352-3026(20)30216-7;
- Perico L., Benigni A., Casiraghi F. et al. (2021). Immunity, endothelial injury and complement-induced coagulopathy in COVID-19. *Nat Rev Nephrol*, 17:46–64. doi:10.1038/s41581-020-00357-4;
- Sheu JR., Hsiao G., Shen M-Y. et al. (2002). Mechanisms involved in the antiplatelet activity of magnesium in human platelets. *Br J Haematol*, 2002;119:1033-1041; doi:10.1046/j.1365-2141.2002.03967.x;

24. Sarvazad H., Cahngaripour SH., Eskandari Roozbahani N., Izadi B. (2020). Evaluation of electrolyte status of sodium, potassium and magnesium and fasting blood sugar at the initial admission of individuals with COVID-19 without underlying disease in Golestan Hospital. *Kermanshah New Microbes New Infect*, 38:100807. doi:10.1016/j.nmni.2020.100807;
25. Wallace TC. (2020). Combating COVID-19 and building immune resilience: a potential role for magnesium nutrition? *J Am Coll Nutr*, 39:685-693. doi:10.1080/07315724.2020.1785971;
26. Pour OB., Yahyavi Y., Karimi A., Khamaneh AM., Milani M., Khalili M., Sharifi A. (2021). Serum trace elements levels and clinical outcomes among Iranian COVID-19 patients. *Int J Infect Dis*, 111:164-168. doi: 10.1016/j.ijid.2021.08.053;
27. Wessels I., Rolles B., Rink L. (2020). The potential impact of zinc supplementation on COVID-19 pathogenesis. *Front Immunol*, 11:1712. doi:10.3389/fimmu.2020.01712;
28. Wessels I., Rolles B., Slusarenko AJ., Rink L. (2022). Zinc deficiency as a possible risk factor for increased susceptibility and severe progression of Corona Virus Disease 19. *Br J Nutr*, 127(2):214-232. doi:10.1017/S0007114521000738;
29. Hoang BX., Han B. (2020). A possible application of hinokitiol as a natural zinc ionophore and anti-infective agent for the prevention and treatment of COVID-19 and viral infections. *Med Hypotheses*, 145:110333. doi:10.1016/j.mehy.2020.110333;
30. Fan L., Cui Y., Liu Z., Guo J., Gong X., Zhang Y., Tang W., Zhao J., Xue Q. (2023). Zinc and selenium status in coronavirus disease 2019. *BioMetals*, 19:53:45. doi:10.1007/s10534-023-00501-0;
31. Derwand R., Scholz M., Zelenko V. (2020). COVID-19 outpatients: early risk-stratified treatment with zinc plus low-dose hydroxychloroquine and azithromycin: a retrospective case series study. *Int J Antimicrob Agents*, 56(6):106214. doi:10.1016/j.ijantimicag.2020.106214;
32. Jothimani D., Venugopal R., Abedin MF., Kaliamoorthy I., Rela M. (2020). COVID-19 and the liver. *Journal of Hepatology*, vol. 73, 1231–1240. doi:10.1016/j.jhep.2020.06.006;
33. Im JH., Je YS., Baek J., Chung MH., Kwon HY., Lee JS. (2020). Nutritional status of patients with COVID-19. *Int J Infect Dis*, 100:390-393. doi:10.1016/j.ijid.2020.08.018;
34. Talha KA., Patwary MI., Alam ZN., Ali SM., Ahmed S., Nafee A., Selina F., Khan MH., Shusmita FR., Avi SG., Rahman MN. (2022). Case-Control Study to Evaluate Zinc Deficiency as a Risk Factor for Oxygen Requirement in Patients with COVID-19. *Mymensingh Med J*, 31(1):216-222. PMID: 34999705;
35. Shang W., Dong J., Ren Y., Tian M., Li W., Hu J., Li Y. (2020). The value of clinical parameters in predicting the severity of COVID-19. *J Med Virol*, 92(10):2188–2192. doi:10.1002/jmv.26031;
36. Patel O., Chinni V., El-Khoury J., Perera M., Neto AS., McDonald C., See E., Jones D., Bolton D., Bellomo R., Trubiano J., Ischia J. (2021). A pilot double-blind safety and feasibility randomized controlled trial of high-dose intravenous zinc in hospitalized COVID-19 patients. *J Med Virol*, 93(5):3261-3267. doi:10.1002/jmv.26895;
37. Abd-Elsalam S., Soliman S., Esmail ES., Khalaf M., Mostafa EF., Medhat MA., Ahmed OA., El Ghafar MSA., Alborai M., Hassany SM. (2021). Do zinc supplements enhance the clinical efficacy of hydroxychloroquine?: A randomized multicenter trial. *Biol Trace Elem Res*, 199(10):3642-3646. doi:10.1007/s12011-020-02512-1;
38. Thomas S., Patel D., Bittel B., Wolski K., Wang Q., Kumar A., Il'Giovine ZJ., Mehra R., McWilliams C., Nissen SE., Desai MY. (2021). Effect of high-dose zinc and ascorbic acid supplementation vs usual care on symptom length and reduction among ambulatory patients with SARS-CoV-2 infection: the COVID A to Z randomized clinical trial. *JAMA Netw Open*, 4(2):210369. doi:10.1001/jamanetworkopen.2021.0369;
39. Kiran Kumar PVS., Tomo S., Purohit P., Sankanagoudar S., et al. (2023). Comparative Analysis of Serum Zinc, Copper and Magnesium Level and Their Relations in Association with Severity and Mortality in SARS-CoV-2 Patients. *Biological Trace Element Research*, 201(1):23-30. doi: 10.1007/s12011-022-03124-7;
40. Tsuchiya H. (2022). Gustatory and Saliva Secretory Dysfunctions in COVID-19 Patients with Zinc Deficiency. *Life (Basel)*, 12(3):353. doi: 10.3390/life12030353.

Barbara Sokółowska

ul. Siodorska 102, p. 23D

21-500 Biała Podlaska

b.sokolowska@dyd.akademiabialska.pl

