Adv Psychiatry Neurol 2021; 30 (2): 130-140
DOI: https://doi.org/10.5114/ppn.2021.108477

ADVANCES IN PSYCHIATRY & NEUROLOGY
POSTĘPY Psychiatrii i Neurologii

SARS-CoV-2: Nutritional determinants of reducing the risk of infection of the central nervous system

Uwarunkowania żywieniowe zmniejszania ryzyka infekcji ośrodkowego układu nerwowego przez SARS-CoV-2

Lucjan Szponar, Ewa Matczuk

Narodowy Instytut Zdrowia Publicznego PZH – Państwowy Instytut Badawczy, Warszawa, Polska

Correspondence to/Adres do korespondencji:
Ewa Matczuk
Narodowy Instytut Zdrowia Publicznego
PZH – Państwowy Instytut Badawczy
ul. Chocimska 24
Warszawa, Polska
e-mail: ematczuk@pzh.gov.pl

Submitted/Otrzymano: 16.02.2021
Accepted/Przyjęto do druku: 09.04.2021

Abstract

Purpose: The aim of this study is to assess the nutritional determinants that may contribute to potentially reducing the risk of COVID-19 central nervous system infection or, if infection occurs, to experience it in a mild form.

Views: In this study, the authors collected data on nutrients that support traditional drug treatment and potentially reduce central nervous system infections, while also indicating the role they play in the central nervous system (CNS). The article points out that long chain polyunsaturated fatty acids polyunsaturated fatty acids, probiotics and prebiotics, as well as vitamin D selenium and zinc play a role in supporting immune function and reducing the risk of CNS infections.

It should be noted that, due to the novel nature of the SARS-CoV-2 virus, limited number of studies evaluating the potential impact of dietary components on COVID-19 risk reduction or their adjunctive effect on treatment are available. Therefore, further clinical studies are needed to confirm these results.

Conclusions: The dietary habits and nutrients described in the article support medical care, including vaccination and other therapies. They are likely to reduce the risk of CNS SARS-CoV-2 infection. The functioning of the physiological gut-brain axis supported by probiotics, polyphenols, certain minerals such as zinc, selenium and vitamin D consumed with the diet, can probably reduce the cost of COVID-19 treatment on the CNS. Also, nutrients other than those mentioned in the article, including vitamins A, E, B_1, B_6, B_{12} and iron, could potentially reduce the cost of the treatment of this disease.

Key words: COVID-19, LC-PUFA, vitamin D, selenium, zinc.

Streszczenie

Cel: Oszacowanie uwarunkowań żywieniowych mogących przyczynić się do potencjalnego zmniejszania ryzyka infekcji ośrodkowego układu nerwowego w postaci COVID-19 lub, jeśli dojdzie do infekcji, przebycia jej w łagodnej postaci.

Poglądy: W niniejszej pracy autorzy zebrali dane dotyczące składników pokarmowych wspomagających tradycyjne leczenie farmakologiczne i potencjalnie zmniejszających ryzyko infekcji ośrodkowego układu nerwowego, wskazując jednocześnie na rolę, jaką odgrywają one w ośrodkowym układzie nerwowym (OUN). W artykule wskazano, że wielonienasycone kwasy tłuszczowe LC-PUFA, probiotyki, prebiotyki, a także witamina D, selen i cynk odgrywają rolę we wspieraniu funkcji odpornościowych i zmniejszaniu ryzyka infekcji ośrodkowego układu nerwowego. Należy zauważyć, że obecnie, ze względu na nowy charakter wirusa SARS-CoV-2, istnieje ograniczona liczba badań oceniających potencjalny wpływ składników diety na zmniejszenie ryzyka zakażenia się COVID-19 lub ich działanie wspomagające w procesie leczenia. Konieczne są jednak dalsze badania kliniczne w celu potwierdzenia tych wyników.

Wnioski: Wdrożenie opisanych w artykule uwarunkowań żywieniowych może potencjalnie wspomagać leczenie i zmniejszać ryzyko zakażenia OUN przez SARS-CoV-2, co prowadzi do wniosków, że: 1) opisane w artykule nawyki żywieniowe i składniki odżywcze wspierają opiekę medyczną, w tym szczepienia i inne terapie, prawdopodobnie zmniejszają one ryzyko zakażenia OUN SARS-CoV-2; 2) wspieranie funkcjonowania fizjologicznej osi jelito–mózg przez probiotyki, polifenole, niektóre składniki mineralne takie jak: cynk, selen i witamina D, spożywane wraz z dietą, może prawdopodobnie zmniejszyć koszt leczenia pacjentów z infekcją COVID-19 w obszarze OUN. Również inne niż wymienione w artykule składniki odżywcze, w tym: witaminy A, E, B_1, B_6, B_{12} oraz żelazo, mogą potencjalnie przyczynić się do zmniejszenia kosztów leczenia pacjentów z COVID-19.

Słowa kluczowe: COVID-19, LC-PUFA, witamina D, selen, cynk.

INTRODUCTION

The COVID-19 pandemic, which originated in China, is the most extensive pandemic in 100 years, i.e. since the 1918 Spanish Flu epidemic [1]. This comparison seems to be accurate taking into account a similar functioning of non-specific and specific immunity in humans [2]. The accuracy of the above comparison has been confirmed, in research on the population of New York in 1918 and the current situation with regard to the high increase in deaths due to COVID-19 in 2020 [3].

Although the morbidity in both pandemics is mainly connected with the respiratory system, more and more cases are currently reported of COVID-19-induced lesions in the central nervous system (CNS). In a study conducted in China (Wuhan), out of a population of 214 patients with COVID-19, 36.4% had CNS symptoms. On the other hand, in a Spanish study of 841 patients suffering from COVID-19, neurological symptoms were found in 57.4% of the subjects [4].

As reported in the Japanese press on December 29, 2020, data from Wuhan on the number of cases due to COVID-19 were probably greatly underestimated [5]. Some people infected with SARS-CoV-2 experience a sudden deterioration in health. This is probably caused by a cytokine storm resulting from an abnormal, excessive response of the immune system [6].

Diseases such as COVID-19 may increase the risk of premature death due to an overreaction of the body's immune system to the pathogen. When this happens, cytokines – proteins that stimulate other cells in the immune system to respond in specific ways – are rapidly secreted. The functions of cytokines include coordinating the body's response to infection and inducing inflammation. When SARS-CoV-2 enters the lungs, a local immune response is triggered and the production of cytokines results in the attraction of specialized cells to an intensified attack on the virus in the lower airways. In some patients, excessive levels of cytokines are released, which then activate more immune cells, causing hyper-inflammation. This can seriously worsen the patient's condition, leading to premature death.

Pneumonia is a late stage of the disease when it is not so much the virus that is important, but the excessive immune response that has developed in response to it. The virus itself initiates very strong inflammation. The overproduction of cytokines and immune cells increases the risk of high blood pressure. SARS-CoV-2 shows similar neuroinvasive and neuroinflammatory capabilities to SARS-CoV, and these may lead to the same neuropathologies. Cytokine storms may explain why very young people and children, whose immune systems are probably less developed and therefore produce lower levels of inflammatory cytokines, are less often affected by the disease [7, 8].

The study of SARS-CoV-2 coronavirus infections highlights the importance of proper medical treatment using nutrients, especially those with immunomodulatory effects, to support the body's natural immune defences for various viral infections, among other things [9, 10].

The current analysis of the incidence of COVID-19 and the described nutritional conditions occurring in Poland suggest that there are opportunities to reduce the risk of dysfunction of the CNS due to infection and a milder course of these health disorders, with medical care implementing four sets of features in the recommended health-promoting diet:

INTAKE, IN RECOMMENDED AMOUNTS, OF POLYUNSATURATED FATTY ACIDS OF THE OMEGA-3 AND OMEGA-6 FAMILY AND THEIR PRO-ACID DERIVATIVES SUCH AS PROTECTINS, RESOLVINS AND MARESINS (11-14)

In the group of fatty acids from the omega-3 (n-3) family – long chain polyunsaturated fatty acids (LC-PUFA) – docosahexaenoic acid (DHA) plays a particularly important role. It is, among other things, a modulator of the activity of the cerebral microglia, understood as constantly residing macrophages in the brain, which constitute 5% to 12% of all cells of the central nervous system, depending on the brain region examined.

According to the current state of knowledge of the brain, it has been assumed that these are non-neuronal cells representing about 10% of their total collection in an adult human; their number may be 8 billion 400 thousand, as estimated by Azevedo *et al.* [15].

Table 1 presents the current recommendations for daily intake of LC-PUFAs at the 2020 AI (adequate intake) level (USA), in grams/person/day.

For people over 18 years of age, the AI applies only to α-linolenic acid (ALA), as ALA is the only omega-3 family acid that is essential and the IOM has not established specific recommendations for the intake of eicosapentaenoic acid (EPA), DHA and other polyunsaturated fatty acids of the omega-3 family.

In the discussion of CNS nutritional requirements in terms of LC-PUFA the importance of DHA has been highlighted. This acid, by acting on dendritic spikes, facilitates signal transduction into the nerve cell and the actin-rich structures that shape postsynaptic endings [13]. It is possible that the effects DHA on actin may increase the chance of enhancing long-term memory [17]. A 2015 study by Yurko-Mauro *et al.* found that DHA in conjunction with EPA enhanced episodic memory function in older adults [18].

Phospholipids of the membranes of synaptosomes and the synaptic vesicles of the brain's grey matter contain

Table 1. Current recommendations for daily intake of LC-PUFA at the adequate intake (AI; g/person/day) level according to the IOM (16)

	Male	Female	Pregnancy	Lactation
From birth to 6 months*	0.5 g	0.5 g		
7–12 months*	0.5 g	0.5 g		
1–3 years**	0.7 g	0.7 g		
4–8 years**	0.9 g	0.9 g		
9–13 years**	1.2 g	1.0 g		
14–18 years**	1.6 g	1.1 g	1.4 g	1.3 g
19-50 years**	1.6 g	1.1 g	1.4 g	1.3 g
51+ years**	1.6 g	1.1 g		

**Sum of polyunsaturated acids from the omega-3s family, **α-linolenic acid (ALA)*

up to 40% DHA. Its significant content in neuronal cell membranes is essential for the formation of an adequate number of synaptic connections throughout life.

Synapses surrounded by one of the groups of glial cells, the astrocytes, are involved in the transmission of signals between neurons. Repeated transmission of an impulse strengthens synaptic conductivity for extended period. The formation of neuronal networks with increased conductivity is the basis of learning and memory [19].

Moreover, long-chain polyunsaturated fatty acids increase the chances of the proper myelination of CNS axons, which takes place with the participation of oligodendrocytes, e.g. in the prefrontal cortex [20-22].

The higher content of DHA and other polyunsaturated fatty acids in the phospholipids of neuronal cell membranes, as believed so far, also favourably affects the survival of these cells and utilization of these acids as secondary messengers [23]. Their low content or impaired metabolism is one of the causative factors of cognitive decline and, likely, increased risk of some mental health disorders and neurodegenerative processes [24, 25].

The data presented in this paper indicate that LC-PUFA, and especially DHA, exert a beneficial influence on brain activity in many metabolic processes and sites of this complex system. Further studies on the properties of neuronal cell membranes involving DHA and cell membrane phospholipids seem justified.

Phospholipids also have a beneficial effect on the functioning of neuronal cell membranes. They enhance the positive effect on the activity of the brain nervous tissue [22, 26, 27].

In order to strengthen a favourable state of activity of the CNS it is also beneficial to supplement the diet with choline which improves the concentration of phospholipids in the brain and in cell membrane synapses [28, 29].

A fundamental feature of nerve cells, apart from generating action potentials, is their ability to communicate with other neurons or the cells of other tissues. This communication is carried out by means of synapses, i.e. sites of functional contact between cells. The exchange of information at the synapses can occur by electrical or chemical means.

The right combination of nutrients in an average diet also increases the tree-like protuberances (dendrites) which are the anatomical exponent of new synapses responsible for improving cognitive function [30].

The already mentioned DHA is formed in the body from alpha-linolenic acid. It is a component of cell membrane phospholipids, where it undergoes similar transformations to EPA. During foetal life and early childhood, DHA (n-3) and arachidonic acid (AA, n-6) are essential in the formation of a normal structure of phospholipids of the brain and retina. They constitute more than 50% of all fatty acids of the brain's grey matter.

EPA – an unsaturated fatty acid – also belongs to the n-3 family and is formed in the body from alpha-linolenic acid. It is a component of cell membrane phospholipids, where it is a precursor of icosanoids and prostanoids which include prostaglandins, prostacyclins, thromboxanes, and leukotrienes.

A deficiency of n-3 fatty acids in cell membrane phospholipids causes them to be displaced by n-6 fatty acids, causing pro-aggregative processes to take over from anti-aggregative ones, increasing the risk of atherosclerotic lesions in the arteries. It is assumed that the ratio of linoleic acid (n-6) to alpha-linolenic acid (n-3) should be 5 : 1 to 10 : 1. Even a short period of significantly increased supply of n-6 fatty acids in relation to n-3 results in decreased DHA content in the nervous tissue, and its dysfunction [14, 31].

Phospholipids, as natural glycerides, are included in cellular and cytoplasmic membranes. An important representative of phospholipids is lecithin. Contained in soya beans, among other things, it is a mixture of esters of α- and β-glycerophosphoric acids (mainly the latter, β-lecithin) and unsaturated fatty acids. In addition, it contains a choline residue, esterified with phosphoric acid. The most important area of lecithin's influence is the central nervous system. The choline contained in lecithin enhances the ability to concentrate and remember. There are also reports of effective use of lecithin in increasing concentration and memory [32]. Choline is also involved in fat and cholesterol metabolism. This is associated with the presence of polyunsaturated fatty acids in its molecule, which by binding with cholesterol facilitate its transport and removal from the system. Therefore, lecithin has a beneficial effect on reducing the risk of atherosclerosis and vascular disorders, including CNS disorders. For the reasons mentioned above, choline also participates in the formation and maintenance of the proper structure of cell membranes. It also participates in the transmission of signals both within and between cells.

In the human body, lecithin is probably present in each of the vast number of body cells, as a component of cell membranes [33].

According to the estimate of the above-cited authors, the number of these cells, including in differentiated organs, is 3.72×10^{13}. These preliminary estimates are the beginning of further research in this field.

In the set of total body cell counts given above, the number of brain cells in the central nervous system was given after Azevedo *et al.* [15].

The authors estimated this in relation to the brain of an adult weighing 1508 g. These authors' data indicate that the total number of cells in question is 170 billion [15]. This suggests that neurons make up about half of the total set of brain cells. The ratio of neurons to non-neuronal cells is 1.0. The second type of brain cells are non-neuronal cells. Their proportion is more than half of the total set of cells, i.e. 84 billion, 61 million, 983 thousand.

An important and interesting point of view on the significance of DHA as a nutrient that strengthens the functioning of the organism, especially of the brain, has been raised by Bradbury [34].

A sufficient level of DHA content in the diet is highly likely to reduce the risk of developing such neuropsychiatric disorders as psychosis, and unipolar and bipolar affective disorders [34-36].

In 2021, the Journal *Prostaglandins, Leukotrienes and Essential Fatty Acids* presented direct evidence of a positive effect of omega-3 fatty acids in the course of COVID-19. In the study, people with the highest concentration of omega-3 fatty acids in the blood were four times less likely to die from COVID-19 than those with the lowest concentration. The study in medical units confirms the information presented by the authors of this article that DHA and EPA acids show significant anti-inflammatory effects and at the same time reduce the occurrence of cytokine storms [37]. DHA and EPA acids exert a direct influence on the immune response to viral infections, therefore their serum level is extremely important [38, 39].

LIFESTYLE EFFECTS ON THE PHYSIOLOGICAL FUNCTIONING OF THE GUT-BRAIN AXIS

The gut-brain axis, with the involvement of the gut microbiome, is a bidirectional communication pathway that connects the gut bacterial flora to the central nervous system (CNS).

The microbiome influences the CNS mainly by:

- modulating the concentration of pro- and anti-inflammatory cytokines,
- influencing the content of tryptophan, a precursor of serotonin,
- synthesis of numerous neurotransmitters and influence on the expression of their receptors in the brain,
- interactions with the enteric and autonomic nervous system, especially the vagus nerve,
- regulation of the hypothalamic-pituitary-adrenal (HPA) axis response under stress.

The microbiome also probably plays a role in preventing increased permeability of the intestinal barrier under the influence of psychological stress and pro-inflammatory cytokines.

There is ample evidence for a supportive role of the immune system and pro-inflammatory cytokines in the inflammatory pathogenesis of depression.

Obesity, arising from a sedentary lifestyle, in which "low-grade inflammation" is also involved, can play a role in the development of depression [40].

Existing data suggest that prebiotics and probiotics in the daily diet probably diminish the risk of depressive and anxiety disorders. Physiological functioning of the gut-brain axis facilitates the regulation of food intake, reducing the risk of developing obesity and irritable bowel syndrome [41, 42].

A physiologically functioning gastrointestinal microbiome may probably assist in the maintenance of an energy balance that is beneficial to the body [43].

The above-mentioned effects of reducing the risk of the development of obesity through physical activity and proper medical care are highly beneficial in the conditions of the COVID-19 pandemic because patients with obesity show a higher mortality rate than those with normal BMI [44].

Another strengthener of the gut-brain axis against the formation of tissue or organ cell damage is proper nutrition and the resulting physiological functioning of the microbiome Gut-Brain-Microbiome-Axis. Findings published in 2018 state that there is growing evidence of a continuous, integrated, bi-directional interaction between the gastrointestinal tract and the CNS and between the gut microbiome and the brain. This integration promotes a continuous interaction between the central nervous system, the digestive system and the immune system. Preclinical and clinical studies (Level C) show that the interaction promotes not only a reduced risk of gastrointestinal health disorders but also psychiatric disorders such as autism anxiety, depressive states and many others.

In summarizing the role of probiotics and prebiotics in reducing the incidence of heavy COVID-19 disease the authors wish to point out that studies show that some patients with COVID-19 have significant dysbiosis in probiotic gut microbiota, such as *Lactobacillus* or/and *Bifidobacterium* [45]. In addition, some reports suggest a thesis that requires, in our opinion, further medical investigation of a connection between intestinal microflora, secondary intestinal infection and COVID-19 disease [46-48].

Systematic consumption in the daily diet of prebiotics, probiotics, polyunsaturated long-chain fatty acids and a variety of vegetables, high in dietary fibre and antioxidant vitamins, probably increases the chances of a protective effect of diet against viral infections [49, 50].

Similar views on the beneficial effects of the brain-gut-microbiome-axis in supporting COVID-19 risk reduction through medical care and diet are offered by Joggers, Dhar, and Baghbani [50-52].

THE AVAILABILITY IN STANDARD DIETS OF RECOMMENDED AMOUNTS OF POLYPHENOLS'

Preclinical studies suggest that polyphenols may play a role in reducing the risk of COVID-19-induced health disorders, and also support the body's treatment of the conditions that have occurred by taking these compounds with daily diets [53].

Compounds of this group are present in food products mainly in the form of esters, glycosides or polymers, which the body cannot assimilate in their initial form. Most compounds in glycosylated form are not hydrolysed in the stomach. Flavonoids, such as quercetin, are absorbed in the stomach, but only in their non-glycosylated form. An exception among polyphenols are anthocyanins, whose glycosylated forms predominate in the human body over aglycones (anthocyanidins). Other compounds are hydrolysed by intestinal enzymes or broken down by intestinal microflora. Polyphenols that are not absorbed in the small intestine enter the colon, where they are hydrolysed by gut microflora in glycosylated form. The resulting aglycones are then converted to aromatic acids. A very important part of the activity of polyphenols is their protective effect in relation to the endothelium of damaged blood vessels [54].

Polyphenols have many beneficial properties for reducing the risk of atherosclerosis, brain dysfunction, stroke, cardiovascular disease and cancer [55].

Phytotherapy treatment through antiviral, anti-inflammatory activity reduces the risk of obesity, type II diabetes, and blood clots, and the use of prebiotics reduces the potential risk of adverse health effects in general [56].

Furthermore, polyphenols therapeutic potential should be investigated, at the molecular level towards in reduction of the risk of infection by SARS-CoV-2.

The primary potential mechanism of action of polyphenols realised in medical centres is due to their promising therapeutic potential antiviral activity and immune regulatory function against COVID-19 disease.

Researchers in medical units hope that new studies will soon emerge that will prove to be as important as those from this year demonstrating the role of, for example, epigallocatechin gallate (EGCG), a green tea polyphenol that inhibits the 3CL protease SARS-CoV-2. Results indicate that EGCG inhibits coronavirus replication [57]. The results of another study found promising antiviral effects of curcumin and its analogues, such as inhibition of SARS-CoV-2 virus binding to the host ACE-2 receptor, and host defence against the cytokine storm effect [58].

ZINC, SELENIUM AND VITAMIN D

Evidence shows that zinc, vitamin D and vitamin C individually or in combination improve the immune response. An adequate intake of zinc and vitamins C and D during the COVID-19 pandemic is a promising prophylactic tool due to the high demand for these nutrients in virus contact and the inflammation process.

In the human body, zinc is involved in about 100 enzymes, among other reasons to maintain the structural integrity of proteins in the regulation of gene expression.

Dietary zinc supplementation in economically deprived populations strongly enhances physiological linear growth in children before 5 years of age [59].

According to Rivera [60], zinc deficiency, at the cellular and subcellular level, can lead to disorders in gene transcription, enzyme function, hormone receptor regulation, growth disorders, immunity, neurobehavioral development and fetal development. According to the same team of authors, if, in the population assessed, there are more than 20% of cases of too low a level of daily intake, there is a high risk of deficiency of this nutrient.

Dietary zinc deficiency affects approximately 30% of the world population [61]. In the authors' own study of the diet of the Polish population conducted in 2000-2003, including the assessment of the zinc content, two methods of data collection were applied simultaneously: a questionnaire for the assessment of the whole-day diet from 24 hours preceding the day of data collection with the use of an interview questionnaire, and the use of household budget surveys by the Central Statistical Office. In these studies representative data were obtained, among other things, on the zinc content of 36 163 average whole-day diets of the Polish population. In this population, the zinc content in household budgets was 9.3 mg/person/day and in the dietary interview 9.4 mg/person/day. It was found that the deficiency of this dietary component in the population of households was characteristic, in median values, of 67% of the respondents [62]. These deficiencies concerned boys and girls up to the age of 12 years. However, starting from the 13th year, they primarily concerned the female population. In boys over 16 and men up to 60 years of age, the zinc intake was approximately 5% higher than recommended. In contrast, dietary zinc intakes > 60 years of age were lower than recommended in both sexes by about 15-20%.

In the 2017 Dietary Standards for Polish population set by National Food and Nutrition Institute, the Recommended Dietary Allowance (RDA) for zinc was 11 mg/person/day for men, 8.0 mg/person/day for women. A comprehensive dietary study on dietary zinc intake was published in 2004 for about 180 countries worldwide [63]. In the above-mentioned study, the average zinc intake in Poland was 12.5 mg/person/day.

Since the degree of zinc bioavailability from a whole-day diet seems to be determined by the content of phytic acid, and probably to a lesser extent by dietary fibre, the content of the latter was compared in the same study in analogous age ranges. It was assumed that the recommended dietary fibre content for an adult is 25 g/person/day. The content of dietary fibre for the whole population of boys and men was 25.5 g per average person, with a range from children 1-3 years in the median value of 10.7 g/person/day to 22.7 g/person/day at age > 60 years. In girls and women, the dietary fibre content ingested by the average female was 18.4 g/person/day with a range from 10.1 g/person/day at age 1-3 years to a range of 18.4 g/person/day in the median value for age > 60 years. It seems likely, assuming that the fibre composition of the diets of the average man and woman was similar, that the reduction in zinc bioavailability in men and women was probably similar. The limitation of this comparison is the fact that phytic acid is an unabsorbable dietary component, present in the highest amounts in the average ration in products such as sesame, Brazil nuts, tofu, hazelnuts, almonds, soy beverages, avocado, and buckwheat groats [64]. However, in relation to dietary fibre, we make a distinction between its non-water soluble and soluble parts [65, 66]. Additionally, phytate, which is present in staple foods like cereals, corn and rice, has a strong negative effect on zinc absorption from composite meals. Inositol hexaphosphates and pentaphosphates are the phytate forms that exert these negative effects, whereas the lower phosphates have no or little effect on zinc absorption.

The body zinc content of an adult ranges from 1.5 to 2.5 g, with a higher average content in men than in women. It is present in all organs, tissues, body fluids and secretions. Zinc also has possible antioxidant and inflammation-reducing properties where COVID-19 is concerned [68]. Zinc absorption in humans takes place in the small intestine. This is one of the main mechanisms of systemic homeostasis of this mineral, which is essential for the maintenance of health and is present in humans in trace amounts. Its transport in the body takes place with the participation of the intestinal epithelium and the circulatory system. By far the biggest proportion of this process takes place with the participation of the epithelial cell line Caco-2 [67]. Zinc has prophylactic and supportive properties for the treatment of the aforementioned virus infection [68]. The data presented in this material concerning the zinc content in the all-day diet in Poland have shown that in an average man, the median value of zinc was 11.89 mg/person/day and in an average woman, 8.15 mg/person/day. A deficiency of this nutrient was highly likely to occur more frequently in women than in men.

Zinc finger proteins are among the most numerous groups of proteins and have a wide range of molecular functions. They are able to interact with DNA, RNA, PAR (poly-ADP-ribose) and other proteins [69]. These proteins are involved in many important cellular processes, including genetic transcription, protein translation, metabolism, the folding and assembly of other proteins and lipids, programming of cell death, ubiquitin-mediated protein degradation, signal transduction, DNA repair and cell migration.

Recent medical research evidence suggests that SARS-CoV-2 with severe acute respiratory syndrome is highly sensitive to interferons. A zinc finger antiviral protein that specifically targets CpG dinucleotides in viral RNA sequences blocks SARS-CoV-2. All type I, II and III interferons strongly inhibit SARS-CoV-2 and induce the expression of zinc finger proteins. Low levels of zinc finger proteins significantly increase SARS-CoV production in lung cells, especially after interferon treatment [70].

Serum zinc levels have been positively correlated with healthy lung function, as high zinc levels have been shown to improve lung tolerance to damage from mechanical ventilation [71]. At the same time, it has been shown that the pneumonia mortality rate in elderly patients with zinc deficiency was twice as high compared to patients with normal zinc levels [72].

The risk of zinc deficiency increases in populations consuming low amounts of meat, with a high intake of phytate and fibre, which reduce the bioavailability of zinc, and a high prevalence of diarrhoeal conditions. Based on the existing, if incomplete, epidemiological diagnosis, it seems that Poland does not belong to this group of countries, and the consumption of meat and meat products, at the level of more than 65 kg/person/year, should be assessed as similar to that observed in economically developed countries. A meta-analysis of zinc content in tissues and body fluids by Lowe [73] indicates that zinc is not present in the body in the form of reserves that could be easily activated under deficiency conditions. There is a highly efficient mechanism in the body to maintain homeostasis for zinc by, among other things, increasing its assimilability in the gastrointestinal tract and decreasing its excretion in faeces and urine. In conditions of zinc deficiency in the diet, the application of the technique of tracing the uptake of labelled zinc allowed researchers to establish that when the dietary zinc intake per day decreases from 12.2 mg/day to 0.23 mg/day, the zinc uptake increases in adult men by approximately 100%. At the same time, urinary zinc excretion decreases from 0.36 mg/day to 0.006 mg/day and faecal excretion decreases from 11.8 mg/day to 0.23 mg/day. These results may indicate that deficiencies of this element in some diets may be reduced by increasing its bioavailability and decreasing its excretion in faeces and urine.

The results of our own studies on zinc content in the diet were also compared with the results of studies in 9 European countries involving the populations of women who were surveyed in 2000. These data show that the zinc content in the whole daily diets of adult women in Poland at the level of average intake amounted to 8.8 mg/per capita/day, ranking fourth out of the 8 countries analysed for this particular nutrient. The highest mean zinc intake with a whole-day diet, of 10.9 mg/person/day, was found in the female population in Germany and the lowest, 7.2 mg/person/day, in Ireland.

The analysis of data on zinc content in body fluids and tissues described in 46 collected publications shows that, in healthy subjects, zinc concentrations in plasma, urine and hair are among the reliable biomarkers for zinc content in the body.

According to previous medical studies, a deficiency of this nutrient in the total daily diet is known to be one of the causes of severe COVID-19 disease.

Selenium is a mineral component with an important role in reducing the risk of immune system dysfunction, physiological thyroid function, and oxido-reductive system dysfunction [74, 75]. It occurs in the body in association with methionine and cysteine. Selenocysteine is formed as a result of the exchange of a sulphur atom from the amino acid cysteine into a selenium atom supplied with the diet. These compounds are involved in the formation of key enzymes: glutathione peroxidase, thioredoxin reductase, iodothyronine deionidase, or selenoprotein such as selenoprotein P. There are 25 known selenoproteins, most of which show antioxidant properties such as glutathione peroxidase. Viruses produce reactive oxygen species. For this, adequate levels of glutathione peroxidase and selenoproteins are required in the body and are thought to reduce the risk of inflammation caused by viruses by slowing their replication and mutation [76]. Studies on mice show that selenium deficiency caused by low dietary supply results in reduced glutathione peroxidase activity, which translates into more severe symptoms of viral diseases and longer infection times [76]. Poland, as well as many other European countries, has low selenium levels in the environment and especially in soil. Therefore, selenium deficiency probably occurs in the general population and among patients with viral infections. This causes increased production of reactive oxygen species, which in turn leads to increased oxidative stress, promoting a weakened immune response, viral mutations and increased virulence [77]. During the ongoing pandemic in China, it was observed that in the city of Enshi, which has one of the highest selenium intakes in the world, the recovery rate of people with COVID-19 was almost three times higher than the average for other cities in Hubei province, including Wuhan. For this reason, researchers began to look at this ingredient more closely. In a study in South Korea involving patients with COVID-19, a deficiency of this mineral has been shown to be associated with high SARS virulence. Very low serum selenium levels were present in 44.4% of patients. Among those who died from COVID-19, 65% had low selenium levels, compared to 39% of survivors. This seems to indicate that selenium deficiency weakens the immune system, which increases the frequency of severe disease [78]. These data are in line with previous studies conducted in those infected with the influenza, polio and Coxsackie B3 viruses. Selenium deficiency was shown to be associated with higher mutation rates. The Moghaddam study found that the risk of mortality from septicaemia was inversely proportional to the level of selenium in the body. Serum selenium levels have also been shown to be an important indicator of survival among patients with COVID-19. According to EFSA recommendations, the intake of selenium at the AI level should be 70 μg/day in adult men and women. The mean selenoprotein P level in COVID-19 patients was at 53.3 ± 16.2 μg, lower than EFSA recommendations, and was an indicator of high survival in COVID-19 patients, whereas a level of 40.8 ± 8.1 μg was associated with a significant reduction [79].

In view of the above data, selenium supplementation should be potentially considered in patients with viral infections, given the fact of an enhanced immune response which could contribute to a milder course of COVID-19 disease [80]. Selenium intake at physiologically recommended levels has been shown to be associated with telomere length in adults [81]. Rich sources of selenium include Brazil nuts, seafood and offal as well as meat, cereals and dairy products. Selenium concentrations in foods of plant origin vary considerably depending on geographical location. Excess selenium is toxic. A garlic-like smell on the breath and a metallic taste in the mouth are the first symptoms that may indicate an excess of selenium in the body. The most common clinical signs of chronically high selenium intake or selenosis are hair and nail loss or brittleness. Selenium as a nutrient, in the form of supplements, promotes the proliferation and differentiation of T lymphocytes, thus supporting the immune response, inhibiting the entry of viruses into healthy cells and reducing and their infectious potential [82].

Vitamin D is a very important fat-soluble nutrient with diverse effects on the whole body, including the CNS, and it is also a prohormone acting on a number of genes. Calcitriol, the active (hormonal) form of vitamin D, due to its action belonging to a family of hormones that are transcription factors for target protein genes. Unlike other hormones e.g. androgens, estrogens, glucocorticosteroids, mineralocorticosteroids, and progesterone, the synthesis of calcitriol is limited by the availability of the vitamin D substrate 25-hydroxyvitamin D. The evidence linking vitamin D deficiency to COVID-19 severity is circumstantial but significant. Its frequent deficiency at the brain level increases the risk, starting during fetal life, of cognitive decline, increased risk of developing Alzheimer's disease, schizophrenia, depression, multiple sclerosis, periodic affective disorder, Parkinson's disease, autism, stroke and epilepsy [83]. At the same time, it is noted that the severe course of COVID-19 affects to a greater extent elderly people or patients who live in social care homes and have significant vitamin D deficiencies.

Ergocalciferol is produced in yeast and plants by UVB radiation, and cholecalciferol is found in oily fish and cod liver oil. It is also produced in human skin. Getting enough vitamin D from food is very difficult. Oily fish is the only significant food source. In the conditions of the COVID-19 pandemic, vitamin D deficiency is particularly unfavourable as it increases the risk of, among other things, microglia inflammation, while also increasing the risk of viral infections [84]. A meta-analysis of 25 randomised trials showed a reduction from 42.2% to 40.3% in the risk of one or more upper respiratory tract infections with prior vitamin D supplementation [85]. The decrease in infection rates was greater, from 55% to 40.5%, among those with vitamin D deficiency at the start of the study. The benefit was evident with regular daily vitamin D administration, whichunder the conditions described, reduces, by strengthening the immune system, the risk of a cytokine storm. One of the many functions of vitamin D is to modulate the activity of the immune system. The vitamin interacts with most cellular immune systems, such as macrophages and B and T lymphocytes, and inhibits the formation of pro-inflammatory cytokines [86]. Nothing is lost but a great deal is gained by recommending vitamin D supplementation for all at 800-1000 IU daily. People who are deficient in it should take 4000 IU/day each day, while monitoring their serum levels. Those who are hospitalised for COVID-19 disease should take high doses of this vitamin, depending on their condition [85].

It should be noted that while data from multiple randomized clinical trials or meta-analyses (Level A) for polyunsaturated fatty acids, vitamin D, zinc exist in terms of their anti-inflammatory and immunomodulatory properties, at this time, because SARS-CoV-2 is an emerging virus, there are only a limited number of studies (Level B) evaluating the potential effect of dietary components on COVID-19 risk reduction or their supportive effect in the treatment process. Preliminary data suggest that supplementation with the components discussed in this article may be beneficial in improving the health of patients with viral infections. However, further clinical trials are needed to confirm these results and make possible recommendations against COVID-19 [87].

Implementation of the nutritional conditioning described above may potentially support the treatment and lower the risk of CNS infection via SARS-CoV-2, leading to the overall conclusion that:

1) The dietary habits and nutrients described in the article support medical care, including vaccinations and other therapies. They are probably reducing the risk of SARS-CoV-2 infection of the CNS.

2) The functioning of the physiological gut-brain axis supported by probiotics, polyphenols, and certain minerals such as zinc, selenium and vitamin D consumed as dietary supplements probably may reduce the cost of COVID-19 treatment for complications involving the CNS. Also, nutrients other than those mentioned in the article, including vitamin A, vitamin E, vitamin B_1, vitamin B_6, vitamin B_{12}, and iron, may potentially help to reduce the cost of the treatment of this disease.

Conflict of interest

Absent.

Financial support

Absent.

References

1. Ellul MA, Benjamin L, Singh B, Lant S, Michael BD, Easton A, et al. Neurological associations of COVID-19. Lancet Neurol 2020; 19: 767-783.

2. Konturek S. Fizjologia człowieka: podręcznik dla studentów medycyny, 2nd ed, Wrocław: Elsevier Urban & Partner; 2013, p. 57-148.
3. Faust J, Meng XL, Vittert L. A Conversation on COVID-19 with Brief19 Editor-in-Chief and ER Physician Jeremy Faust. Harvard Data Science Review. 2020.
4. Pezzini A, Padovani A. Lifting the mask on neurological manifestations of COVID-19. Nat Rev Neurol 2020; 16: 636-644.
5. Wuhan's COVID-19 cases may have been 10 times higher, study shows. www.japantimes.co.jp/news/2020/12/29/asia-pacific/wuhan-china-coronavirus-study/.
6. Mehta P, Mcauley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020; 395: 1033-1034.
7. Janik M. Infekcje wirusem SARS-CoV-2 a zjawisko burzy cytokinowej. https://euroimmun.pl/blog/infekcje-wirusem-sars-cov-2-a-zjawisko-burzy-cytokinowej/.
8. Yachou Y, El Idrissi A, Belapasov V, Ait Benali S. Neuroinvasion, neurotropic, and neuroinflammatory events of SARS-CoV-2: understanding the neurological manifestations in COVID-19 patients. Neurol Sci 2020; 41: 2657-2669.
9. Iadecola C, Anrather J, Kamel H. Effects of COVID-19 on the Nervous System. Cell 2020; 183: 16-27.
10. Mishra R, Banerjea AC. Neurological damage by coronaviruses: a catastrophe in the queue! Front Immunol 2020; 10: 565521.
11. Li QF, Hao H, Tu WS, Guo N, Zhou XY. Maresins: anti-inflammatory pro-resolving mediators with therapeutic potential. Eur Rev Med Pharmacol Sci 2020; 24: 7442-7453.
12. Duvall MG, Levy BD. DHA- and EPA-derived resolvins, protectins, and maresins in airway inflammation. Eur J Pharmacol 2016; 15: 144-155.
13. Chang PK, Khatchadourian A, McKinney RA, Maysinger D. Docosahexaenoic acid (DHA): a modulator of microglia activity and dendritic spine morphology. J Neuroinflammation 2015; 22: 34.
14. Jarosz M, et al. Normy żywienia dla populacji Polski. Warszawa: Instytut Żywności i Żywienia; 2017, p. 56-71.
15. Azevedo FA, Carvalho LR, Grinberg LT, Farfel JM, Ferretti RE, Leite RE, et al. Equal numbers of neuronal and nonneuronal cells make the human brain an isometrically scaled-up primate brain. J Comp Neurol 2009; 10: 532-541.
16. Institute of Medicine, Food and Nutrition Board Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids (macronutrients). Washington, DC: National Academy Press; 2005.
17. Basu S, Lamprecht R. The Role of actin cytoskeleton in dendritic spines in the maintenance of long-term memory. Front Mol Neurosci 2018; 1: 11-143.
18. Yurko-Mauro K, Alexander DD, Van Elswyk ME. Docosahexaenoic acid and adult memory: a systematic review and meta-analysis. PLoS One 2015; 10: e0120391.
19. Lee S, Zhang H, Webb D. Dendritic spine morphology and dynamics in health and disease. Cell Health and Cytoskeleton 2015; 7: 121-131.
20. Georgieff MK. Nutrition and the developing brain: nutrient priorities and measurement. Am J Clin Nutr 2007; 85: 614S-620S.
21. Williamson JM, Lyons DA. Myelin dynamics throughout life: an ever-changing landscape? Front Cell Neurosci 2018; 12: 424.
22. Squire LR, Berg D, Bloom FE, du Lac S, Ghosh A, Spitzer NC. Fundamental Neuroscience. 4th ed. Waltham: Academic Press (Elsevier); 2013.
23. Falomir-Lockhart LJ, Cavazzutti GF, Giménez E, Toscani AM. Fatty acid signaling mechanisms in neural cells: fatty acid receptors. Front Cell Neurosci 2019; 13: 162.
24. Cutuli D. Functional and structural benefits induced by omega-3 polyunsaturated fatty acids during aging. Curr Neuropharmacol 2017; 15: 534-542.
25. Jaworski J. Białka z rodziny +TIP – „agenci" śledzący mikrotubule w rozwoju i plastyczności neuronów. Kosmos: Problemy Nauk Biologicznych 2018; 67: 2374.
26. Hussain G, Anwar H, Rasul A, Imran A, Qasim M, Zafar S, et al. Lipids as biomarkers of brain disorders. Crit Rev Food Sci Nutr 2020; 60: 351-374.
27. Walczewska A, Stępień T, Bewicz-Binkowska D, Zgórzyńska E. Rola kwasu dokozaheksaenowego w czynności komórek nerwowych. Postepy Hig Med Dosw 2011; 65: 314-327.
28. Sanders LM, Zeisel SH. Choline: dietary requirements and role in brain development. Nutr Today 2007; 42: 181-186.
29. Tayebati SK, Amenta F. Choline-containing phospholipids: relevance to brain functional pathways. Clin Chem Lab Med 2013; 51: 513-521.
30. Szczygieł B, Gaweł M, Ukleja A, Boniecka I. Rola wybranych składników odżywczych we wspomaganiu leczenia farmakologicznego choroby Alzheimera. Medycyna Wieku Podeszłego 2014; 4: 7-15.
31. Kolanowski W. Funkcje i przemiany metaboliczne wielonienasyconych kwasów tłuszczowych omega-3 w organizmie człowieka. Bromat Chem Toksykol 2013; 46: 267-278.
32. Moré MI, Freitas U, Rutenberg D. Positive effects of soy lecithin-derived phosphatidylserine plus phosphatidic acid on memory, cognition, daily functioning, and mood in elderly patients with Alzheimer's disease and dementia. Adv Therapy 2014; 31: 1247-1262.
33. Bianconi E, Piovesan A, Facchin F, Beraudi A, Casadei R, Frabetti F, et al. An estimation of the number of cells in the human body. Ann Hum Biol 2013; 40: 463-471.

34. Bradbury J. Docosahexaenoic acid (DHA): an ancient nutrient for the modern human brain. Nutrients 2011; 3: 529-554.
35. Dudek D, Siwek M, Rybakowski J (eds.).Choroba afektywna dwubiegunowa – wyzwania terapeutyczne. Poznań: Termedia Wydawnictwa Medyczne; 2013.
36. Rabe-Jabłońska J. Zaburzenie obsesyjno-kompulsyjne. Zaburzenie dysocjacyjne (konwersyjne). In: Namysłowska I (ed.). Psychiatria dzieci i młodzieży. Warszawa: Wydawnictwo Lekarskie PZWL; 2012.
37. Asher A, Tintle NL, Myers M, Lockshon L, Bacareza H, Harris WS. Blood omega-3 fatty acids and death from COVID-19: a pilot study. Prostaglandins Leukot Essent Fatty Acids 2021; 166: 102250.
38. Calder PC. Nutrition, immunity and COVID-19. BMJ Nutr Prev Health 2020; 20: 74-92.
39. Messina G, Polito R, Monda V, Cipolloni L, Di Nunno N, Di Mizio G, et al. Functional role of dietary intervention to improve the outcome of COVID-19: a hypothesis of work. Int J Mol Sci 2020; 28: 3104.
40. Luppino FS, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BW, Zitman FG. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry 2010; 67: 220-229.
41. Rudzki L, Frank M, Szulc A, Gałęcka M, Szachta P, Barwinek D. Od jelit do depresji – rola zaburzeń ciągłości bariery jelitowej i następcza aktywacja układu immunologicznego w zapalnej hipoteziedepresji. Neuropsychiatr Neuropsychol 2012; 7: 76-84.
42. Osadchiy V, Martin CR, Mayer EA. The gut-brain axis and the microbiome: mechanisms and clinical implications. Clin Gastroenterol Hepatol 2019; 17: 322-332.
43. Jumpertz R, Le DS, Turnbaugh PJ, Trinidad C, Bogardus C, Gordon JI, Krakoff J. Energy-balance studies reveal associations between gut microbes, caloric load, and nutrient absorption in humans. Am J Clin Nutr 2011; 94: 58-65.
44. Hussain A, Bhowmik B, do Vale Moreira NC. COVID-19 and diabetes: Knowledge in progress. Diabetes Res Clin Pract 2020; 162: 108142.
45. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020; 8: 420-422.
46. Gu S, Chen Y, Wu Z, Chen Y, Gao H, Lv L, et al. Alterations of the gut microbiota in patients with COVID-19 or H1N1 influenza. Clin Infect Dis 2020; 4: 709.
47. Yeo C, Kaushal S, Yeo D. Enteric involvement of coronaviruses: is faecal-oral transmission of SARS-CoV-2 possible? Lancet Gastroenterol Hepatol 2020; 5: 335-337.
48. Gao QY, Chen YX, Fang JY. 2019 Novel coronavirus infection and gastrointestinal tract. J Dig Dis 2020; 21: 125-126.
49. Martin CR, Osadchiy V, Kalani A, Mayer EA. The brain-gut-microbiome axis. Cell Mol Gastroenterol Hepatol 2018; 6: 133-148.
50. Dhar D, Mohanty A. Gut microbiota and Covid-19-possible link and implications. Virus Res 2020; 285: 198018.
51. Jaggers GK, Watkins BA, Rodriguez RL. COVID-19: repositioning nutrition research for the next pandemic. Nutr Res 2020; 81: 1-6.
52. Baghbani T, Nikzad H, Azadbakht J, Izadpanah F, Kashani HH. Dual and mutual interaction between microbiota and viral infections: a possible treat for COVID-19. Microb Cell Fact 2020; 26: 217.
53. Khalil A, Tazeddinova D. The upshot of Polyphenolic compounds on immunity amid COVID19 pandemic and other emerging communicable diseases: an appraisal. Nat Prod Bioprospect 2020; 10: 411-429.
54. Paszkiewicz M, Budzyńska A, Różalska B, Sadowska B. Immunomodulacyjna rola polifenoli roślinnych. Postepy Hig Med Dosw 2012; 66: 637-646.
55. Tressera-Rimbau A, Arranz S, Eder M, Vallverdú-Queralt A. Dietary polyphenols in the prevention of stroke. Oxid Med Cell Longev 2017; 2017: 7467962.
56. Levy E, Delvin E, Marcil V, Spahis S. Can phytotherapy with polyphenols serve as a powerful approach for the prevention and therapy tool of novel coronavirus disease 2019 (COVID-19)? Am J Physiol Endocrinol Metab 2020; 319: 689-708.
57. Jang M, Park R, Park YI, Cha YE, Yamamoto A, Lee JI, Park J. EGCG, a green tea polyphenol, inhibits human coronavirus replication in vitro. Biochem Biophys Res Commun 2021; 547: 23-28.
58. Noor H, Ikram A, Rathinavel T, Kumarasamy S, Nasir Iqbal M, Bashir Z. Immunomodulatory and anti-cytokine therapeutic potential of curcumin and its derivatives for treating COVID-19 – a computational modelling. J Biomol Struct Dyn 2021; 25: 1-16.
59. Imdad A, Bhutta ZA. Effect of preventive zinc supplementation on linear growth in children under 5 years of age in developing countries: a meta-analysis of studies for input to the lives saved tool. BMC Public Health 2011; 13 Suppl 3: 22.
60. Rivera J, Brown KH, Hotz C, Ruel M. Zinc deficiency: issues for public health, assessment, and prevention. Forum Nutr 2003; 56: 59-61.
61. Mońka I, Wiechuła D. Znaczenie cynku dla organizmu ludzkiego w aspekcie suplementacji tego pierwiastka. Ann Acad Med Silesiensis 2017; 71: 314-325.
62. Szponar L, Sekuła W, Rychlik E, et al. Badania indywidualnego spożycia żywności i stanu odżywienia w gospodarstwach domowych. Warszawa: Wydawnictwo GUS; 2003.
63. International Zinc Nutrition Consultative Group (IZiNCG); Brown KH, Rivera JA, Bhutta Z, et al. International Zinc Nutrition Consultative Group (IZiNCG) technical document #1. Assessment of the risk of zinc deficiency in populations and options for its control. Food Nutr Bull 2004; 25 (1 Suppl 2): S99-S203.
64. Humer E, Schedle K. Fermentation of food and feed: a technology for efficient utilization of macro and trace elements in monogastrics. J Trace Elem Med Biol 2016; 37: 69-77.

65. Ciborowska H, Rudnicka A. Dietetyka. Żywienie zdrowego i chorego człowieka. Warszawa: Wydawnictwo PZWL; 2012.
66. Szponar L. Zmniejszanie ryzyka zagrożenia zdrowia kobiet w wieku prokreacyjnym poprzez wpływ na sposób żywienia – założenia do strategii. Rozprawa habilitacyjna. Warszawa: Instytut Żywności i Żywienia; 2013.
67. Maares M, Haase H. A guide to human zinc absorption: general overview and recent advances of in vitro intestinal models. Nutrients 2020; 12: 762.
68. Joachimiak MP. Zinc against COVID-19? Symptom surveillance and deficiency risk groups. PLoS Negl Trop Dis 2021; 15: e0008895.
69. Cassandri M, Smirnov A, Novelli F, Pitolli C, Agostini M, Malewicz M, et al. Zinc-finger proteins in health and disease. Cell Death Discov 2017; 13: 17071.
70. Nchioua R, Kmiec D, Müller JA, Conzelmann C, Groß R, Swanson CM, et al. SARS-CoV-2 is restricted by zinc finger antiviral protein despite preadaptation to the Low-CpG environment in humans. mBio 2020; 11: e01930-20.
71. Boudreault F, Pinilla-Vera M, Englert JA, Kho AT, Isabelle C, Arciniegas AJ, et al. Zinc deficiency primes the lung for ventilator-induced injury. JCI Insight 2017; 2: e86507.
72. Barnett JB, Hamer DH, Meydani SN. Low zinc status: a new risk factor for pneumonia in the elderly? Nutr Rev 2010; 68: 30-37.
73. Lowe NM, Fekete K, Decsi T. Methods of assessment of zinc status in humans: a systematic review. Am J Clin Nutr 2009; 89 (Suppl): 2040S-2051S.
74. Medeiros-Neto G, Rubio IGS. Iodine-deficiency disorders. In: Jameson JL, De Groot LJ, de Kretser DM, et al. (eds.). Endocrinology: Adult and pediatric. 7th ed. Amsterdam: WB Saunders; 2016.
75. Guillin OM, Vindry C, Ohlmann T, Chavatte L. Selenium, selenoproteins and viral infection. Nutrients 2019; 11: 2101.
76. Beck MA, Nelson HK, Shi Q, Van Dael P, Schiffrin EJ, Blum S, et al. Selenium deficiency increases the pathology of an influenza virus infection. FASEB J 2001; 15: 1481-1483.
77. Klecha B, Bukowska B. Selen w organizmie człowieka – charakterystyka pierwiastka i potencjalne zastosowanie terapeutyczne. Bromat Chem Toksykol 2016; 59: 818.
78. Im JH, Je YS, Baek J, Chung MH, Kwon HY, Lee JS. Nutritional status of patients with COVID-19. Int J Infect Dis 2020; 100: 390-393.
79. Moghaddam A, Heller RA, Sun Q, Seelig J, Cherkezov A, Seibert L, et al. Selenium deficiency is associated with mortality risk from COVID-19. Nutrients 2020; 12: 2098.
80. Jayawardena R, Sooriyaarachchi P, Chourdakis M, Jeewandara C, Ranasinghe P. Enhancing immunity in viral infections, with special emphasis on COVID-19: a review. Diabetes Metab Syndr 2020; 14: 367-382.
81. Shu Y, Wu M, Yang S, Wang Y, Li H. Association of dietary selenium intake with telomere length in middle-aged and older adults. Clin Nutr 2020; 39: 3086-3091.
82. Kieliszek M, Lipiński B. Selenium supplementation in the prevention of coronavirus infections (COVID-19). Med Hypotheses 2020; 143: 109878.
83. Annweiler C, Montero-Odasso M, Llewellyn DJ, Richard-Devantoy S, Duque G, Beauchet O. Meta-analysis of memory and executive dysfunctions in relation to vitamin D. J Alzheimers Dis 2013; 37: 147-171.
84. Anjum I, Jaffery SS, Fayyaz M, Samoo Z, Anjum S. The role of vitamin D in Brain health: a mini literature review. Cureus 2018; 10: e2960.
85. Griffin G, Hewison M, Hopkin J, Kenny R, Quinton R, Rhodes J, et al. Vitamin D and COVID-19: evidence and recommendations for supplementation. R Soc Open Sci 2020; 7201912.
86. Biesalski HK. Vitamin D deficiency and co-morbidities in COVID-19 patients – a fatal relationship? Nfs Journal 2020; 20: 10-21.
87. BourBour F, Mirzaei Dahka S, Gholamalizadeh M, Akbari ME, Shadnoush M, Haghighi M, et al. Nutrients in prevention, treatment, and management of viral infections; special focus on coronavirus. Arch Physiol Biochem 2020; 9: 1-10.