

PROGRESS OF RESEARCH IN NUTRITIONAL THERAPY FOR NEW CORONAVIRUS INFECTION (NARRATIVE REVIEW)

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Abstract

Keywords: covid-19, Prevention, Treatment therapy.

Objective: In this review, we highlight the importance of an optimal nutrient status to strengthen the immune system during the COVID-19 crisis, focusing on the most relevant constituents that reduce inflammation and Provide a holistic perspective nutritional therapy the new coronavirus (covid-19) to assist researchers and improving areas for future response plans to deal with these diseases, and to provide a summary of the nutrients that help stop their development.

Methods: This is a theoretical study conducted through a comprehensive review of the literature and research in the research engines (PubMed), (Read) and (ELSEVIER) and other new studies published in Chinese; we obtained information nutritional treatment who contributed to increasing the immunity of patients, due to the lack of treatment for this disease.

Results: Until now no effective drug for the treatment of new coronavirus, pneumonia (covid-19) has been found. The development of vaccines is still in animal experiments. Recommendations and measures to control the spread of infection and nutritional therapy are still the only way to prevent the spread of covid-19 virus. Because, People relied only on treatments that were effective on previous viruses, for example those that have been used during the SARS and MERS epidemics.

Discussion: The Covid-19 virus remains a global concern and more research is needed to control it. In addition, people need to know the nutrition ingredients that have a positive effect on increasing the immunity of the human body.

Introduction

Problem Statement

The outbreak caused by the new coronavirus (covid-19) is very serious, Globally in the past week, rates of new COVID-19 cases and deaths continued to increase, with almost 4 million new cases and 60 000 new deaths recorded. Cumulatively as of 15 November 2020, 53.7 million confirmed cases and 1.3 million deaths have been reported to WHO. Globally in the past week, rates of new COVID-19 cases and deaths continued to increase, with almost 4 million new cases and 60 000 new deaths recorded. Cumulatively as of 15 November 2020, 53.7 million confirmed cases and 1.3 million deaths have been reported to WHO Figure1, Figure2 and Table1 [1]. Covid-19 is a new strain of the virus that has not yet been found in humans and belongs to the coronavirus family, which can cause diseases ranging from the common cold to more serious diseases, such as Middle East respiratory syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS)[2].

According to report epidemic center Guangxi, China has been the center of new virus infections for the past two

decades, the most recent of which is the new Corona virus (Covid-19), which has caused a global crisis and anxiety. Wuhan appeared for unknown reasons. On December 12, 2019, the Wuhan Municipal Health Commission reported 27 cases of viral pneumonia Covid-19. Most of them have been linked to the virus in the Hunan seafood market, where poultry, bats, snakes and other wildlife are also sold.

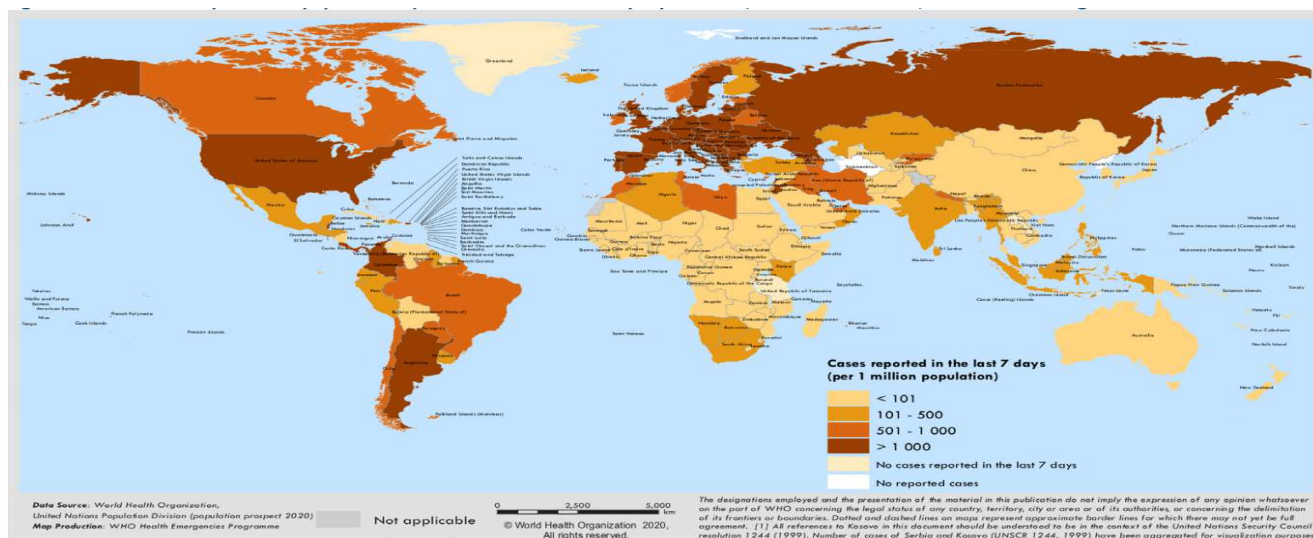
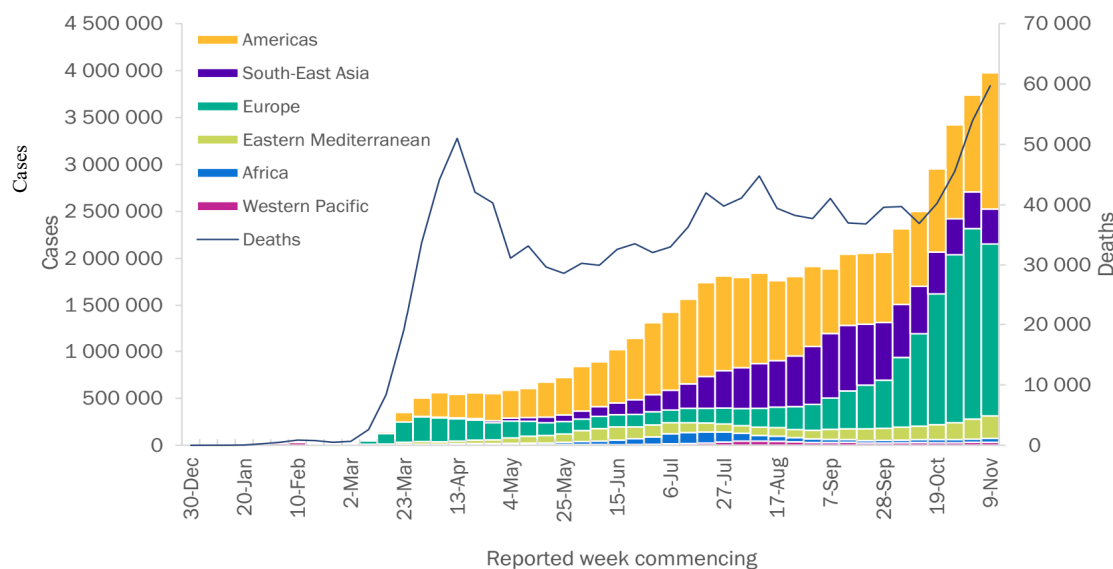


Figure 1. COVID-19 cases per million population reported in the last seven days by countries, territories and areas, 9 November through 15 November 2020



**See data table and figure notes.

Figure 2: COVID-19 cases reported weekly by WHO Region, and global deaths, as of 15 November 2020

Table 1. Newly reported and cumulative COVID-19 confirmed cases and deaths, by WHO Region, as of 15 November 2020

WHO Region	New cases in last 7 days (%)	Change in new cases in last 7 days *	Cumulative cases (%)	New deaths in last 7 days (%)	Change in new deaths in last 7 days*	Cumulative deaths (%)
Europe	1 840 086 (46%)	-10%	15 047 248 (28%)	29 043 (49%)	18%	341 488 (26%)
Americas	1 450 998 (36%)	41%	22 960 102 (43%)	19 106 (32%)	11%	675 735 (52%)
South-East Asia	373 786 (9%)	-4%	10 015 731 (19%)	4 534 (8%)	-12%	153 860 (12%)
Eastern Mediterranean	238 390 (6%)	11%	3 545 801 (7%)	5 747 (10%)	1%	90 052 (7%)
Africa	40 990 (1%)	22%	1 398 935 (3%)	834 (1%)	<1%	31 450 (2%)
Western Pacific	32 973 (1%)	5%	798 170 (1%)	435 (1%)	15%	16 377 (1%)
Global	3 977 223 (100%)	6%	53 766 728 (100%)	59 699 (100%)	11%	1 308 975 (100%)

*Percent change in the number of newly confirmed cases/deaths in past seven days, compared to seven days prior. Regional percentages rounded to the nearest whole number, global totals may not equal 100%.

**See data, table and figure notes

Research questions

1. What is the Covid-19 virus and what is its relationship to previous viruses?
2. What are the nutritional therapy research findings of him so far?
3. What are the most important mechanisms can be taken to reduce infection?
4. What are the most important foods that can increase immunity in patients?

Research Objectives

1. Provide a holistic view nutritional therapy of the Covid-19 virus to help researchers.
2. Improve the areas of action plans and the response to the outbreak.
3. Benefiting from the research results conducted in China and applying them in the areas of the outbreak.
4. Contribute to find appropriate measures to limit and prevent the outbreak.

Research Importance

The importance of the research lies in providing a comprehensive and brief description describing the results achieved on Covid-19 virus in terms of nutritional therapy, and appropriate prevention mechanisms by transferring the results of the experiment from field studies and Researches who conducted at the Virus Spread Center (China), and monitoring the recipes in traditional Chinese medicine.

Research Methodology

This is a theoretical study conducted through a comprehensive review of the literature and research in research engines (PubMed), (Read) and (ELSEVIER) and other new studies published in Chinese, where information was obtained about the diagnosis, treatment, prevention and methods of infection, and in order to determine the same characteristics of the virus (Covid-19), Some studies related to a viruses have been reviewed Middle East respiratory syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS).

Literature Review

Covid-19 overview

New coronavirus (covid-19)

Coronaviruses are enveloped viruses that are positive for single-stranded large RNA viruses and can infect humans as well as a variety of animals. In 1966, Tyrell and Bino first discovered the coronavirus, a family of mammalian origin, in people infected with a flu pandemic. Can infect humans has found seven coronavirus is HCoV-229E, HCoV-OC43, SARS-COV, HCoV-NL63 and HCoV-HKU1, MERS-CoV and newly discovered 2019-nCoV (SARS-HCoV-2), coronavirus subfamily of α , β , γ , and δ [1], beta coronavirus can lead to severe disease and death, and alpha coronavirus can result in asymptomatic or mild symptoms of infection, 2019 new coronavirus is caused by SARS-CoV-2 virus, Sarscov-2 belongs to the b-line of da-coronavirus, which is closely related to sars-cov virus. It is characterized by strong infectivity and high morbidity. The whole-genome level is 96% the same as that of the bat coronavirus, and bats are likely to be the host of the new coronavirus [3].

Ways to spread

The structural analysis of the receptor-binding domain (RBD) of the spike glycoprotein entering the host cell of the coronavirus found that the RBDs of the two viruses 2019-nCoV and SARS-CoV had 72% homologous properties in the amino acid sequence, and the molecular simulation showed a highly similar three-way structure. However, 2019-nCoV has a unique ring, and molecular simulations show that the RBD of 2019-nCoV interacts more strongly with angiotensin-converting enzyme 2 (ACE2). ACE2 is widely expressed in the entire animal world, from fish, amphibians, reptiles, birds to mammals, and has a conservative level of structure. Structural analysis suggests that ACE2 from these animals may bind to RBD from 2019-nCoV, making them possible natural hosts for the virus. 2019-nCoV is thought to be transmitted through respiratory droplets. However, since ACE2 is expressed mainly in the intestines, testes and kidneys, feces-mouth and other routes of transmission are also possible [4].

Previous studies have suggested that the main route of transmission of the virus is the virus droplets in an infected person's cough, which can be transmitted by frequently touching contaminated hands and surfaces. For example, contact with the doorknobs that the patient has come into contact with, as well as the fixed telephone keyboards, bed tables and frames, and other items in the patient's environment, can be transmitted [5]. However, in early cases, the researchers said, they focused on patients with respiratory symptoms and may have overlooked symptoms associated with the digestive tract. A total of 14 patients (10%) of the 138 patients in a hospital in Wuhan city initially developed diarrhea and nausea fever and breathing difficulties the day or two before the onset of the disease [6] This confirms that food has a direct relationship to the virus and cannot be ignored.

The first United States U.S. patient to be diagnosed with 2019-nCoV (COVID-19) also experienced two days of poor defecation, followed by the discovery of the virus in his feces, and other such cases have been recorded on the Lancet, although this is rare, and researchers say feces may be a secondary route of transmission. Recent studies have also found the virus in a patient's urine.

Laboratory examination

Blood routine examination white blood cell count softens usually normal or decreased, accompanied by a decrease in lymphocyte count, severe progressive lymphocytic reduction, C-reactive protein (CRP) normal or elevated, and primary calcium (PCT) normal in most cases. PCT - level 0.5 ng/mL prompt stomps with bacteria. In severe cases, levels of hepatic enzymes, myosin and myoglobin selevate, D-dipolymer levels rise [7].

Etiological examination

Novel coronavirus is an RNA virus. The detection method mainly adopts nucleic acid detection. The collected samples are mainly throat swabs, nasal swabs, alveolar lavage fluid, sputum samples, feces samples, etc. Suspected cases can only be excluded if their respiratory pathogenic nucleic acid tests are negative for two consecutive times (sampling time interval is at least 1 day)[8]. Generally, 140 μ L sample extraction is used for nucleic acid detection. At the beginning of the epidemic, the next generation sequencing was carried out from the bronchoalveolar lavage fluid

samples and culture isolates of 9 hospitalized patients, 8 complete and 2 partial genome sequences of 2019-nCoV were obtained [9], and a PCR detection kit was developed according to the gene sequence of the virus. Nucleic acid sequencing by double extraction of sputum samples and throat swabs from different patients showed that the virus content in sputum samples was higher than that in throat swabs. Compared with throat swabs, sputum samples had better detection effect. If a liquefaction method more conducive to sputum samples could be found, the virus content in sputum samples would be higher and more conducive to laboratory detection [10]. Some studies have compared the detection results of six domestic reagents on nucleic acid samples of patients with weakly positive new crown pneumonia at different periods. It is found that the detection effect of Shuoshi biological novel coronavirus (2019) nucleic acid detection kit (double fluorescence PCR method, batch number: 20200108) and Beijing Zhuocheng Huisheng novel coronavirus (covid-19)ORF1ab/N gene double real-time fluorescence PCR detection kit (batch number: 2020123) is better than the other four[11], but it is still necessary to further compare different batch numbers for detection and analysis of large samples. In order to reduce false negative results in the kit test and improve its sensitivity, the Zhong Nanshan team has newly developed the novel coronavirus IgM antibody rapid detection kit. Through blood testing, the kit has been found to be able to detect a considerable number of patients with negative PCR nucleic acid detection, and has completed preliminary evaluation in laboratory and clinic. It can complement nucleic acid detection and has been sent to Hubei Province in large quantities.

Treatment

Before starting to review the results of research on clinical nutrition, we will review some drugs that have been used to treat some pathologies in Western medicine and in China.

Western medicine treatment

There is no specific novel coronavirus pneumonia treatment. Studies have found that 2019-nCoV and SARS-CoV have high sequence consistency in their RdRp and 3CLpro proteins. However, some effective small molecule therapies based on these two proteins in SARS-CoV have been discovered previously. However, the drug is still in the stage of clinical trials, which may be applied to the treatment of 2019 nCoV patients[13]. The fifth edition of novel coronavirus pneumonia diagnosis and treatment plan issued by China health and Health Commission [14] is that the interferon IFN- is mainly used for IFN- and IFN- beta. Add "or ribavirin" on the basis of lopinavir / ritonavir. Novel coronavirus pneumonia clinical guideline for WHO, published in [15], has not been recommended for the use of corticosteroids in suspected patients. In February 7, 2020 [16] a article published in the lancet magazine also suggested that although corticosteroids were widely used in SARS and MERS treatment, there was not enough evidence that corticosteroids were beneficial to the treatment of respiratory tract infections. Although it can inhibit lung inflammation, it can also inhibit the immune response and prevent the elimination of pathogens. Due to the lack of sufficient evidence, corticosteroid treatment is still controversial and should be used carefully. The broad-spectrum antiviral activity of arbidol (ARB) in vitro and in vivo has been confirmed, but the current evidence only proves that ARB has anti CoVs activity in vitro, and its therapeutic effect on 2019 nCoV still needs the support of clinical experiments [17]. The sixth edition of novel coronavirus pneumonia treatment program released by China health and Health Commission [18] has been added to chloroquine and chloroquine phosphate as a therapeutic drug. The course of treatment is not more than 10 days. A novel coronavirus was introduced to analyze the structure of receptor binding domain (RBD) of spike glycoprotein in the host cells. The study found that the RBD of new coronavirus (covid-19) was mainly combined with ACE2 receptor. It is necessary to develop antibodies and small molecule inhibitors that can block the interaction between ACE2 and RBD to fight against the virus.

Treatment with traditional Chinese medicine (TCM)

This disease belongs to the category of epidemic disease in traditional Chinese medicine, and its basic pathogenesis is characterized by "dampness, heat, toxin and stasis". There are studies in China on the general treatment principle of "dispersing cold and dehumidification, avoiding pollution and turbidity", discussing the treatment and protective measures of TCM by stages, and giving corresponding prescriptions according to different disease stages of patients, the treatment drugs are mainly Atractylodes, Huoxiang, Houpu, Caocao, areca, tangerine peel, ephedra, Qiang Huo and other traditional Chinese medicines [19,20]. Luo Dan and other[21] novel coronavirus pneumoniae theory is combined with the new type of coronavirus pneumonia theory for high-risk groups. As mentioned above, the receptor binding domain (RBD) of spicule glycoprotein that coronaviruses enter host cells has been structurally analyzed.

However, it was found that RBD of novel coronaviruses mainly binds ACE2 receptor, so antibodies and small-molecule inhibitors capable of blocking ACE2's interaction with RBD should be developed to combat this virus [22].

Nutritional therapy

After the outbreak of Covid-19 and spread rapidly. Strict national policies to control the disease have been implemented, including policies to practice social distancing and encouraging or even forcing people to stay at home. Especially during this self-confinement, often perceived as stressful, individuals are frequently at a loss regarding optimal dietary patterns and adequate nutrient status in order to stay healthy. In order to prevent infection, a healthy functional immune system is paramount, and an important foundation for an optimal immune response is an adequate and balanced diet.[23]

Researchers believe that immune response is impaired due to lack of specific nutritional elements [12]. It is suggested that before routine treatment, the nutritional status of each infected patient should be evaluated, and the uninfected population and medical personnel should be vaccinated with existing RNA virus vaccines, including influenza vaccines.

Table 1. Selected studies associating dietary constituents with viral or other infection risk and symptoms.

Study Design	Description	Main Findings	Ref	
Proteins				
1	Human cross-sectional study	23 elderly patients subjected to influenza vaccination and measurement of their nutrient status.	Total protein status (determined by questionnaire) was slightly lower ($p < 0.05$) in influenza vaccine non-responders vs. responders (66 vs. 69 g/L). Similar results were found for iron, proposing that immune-response was compromised by poor nutrient status in this elderly population	[24]
2	Animal study (mice)	Group receiving a diet adequate in protein (AP; 18% of energy) vs. group receiving very low protein (VLP; 2%) for 3 weeks. Both groups were subjected to influenza infection.	Higher mortality in the VLP group ($p < 0.001$) vs. AP, 25 d post infection (p.i.). The AP vs. the VLP group showed a decreased virus titer by day 9 ($p < 0.001$) and an efficient clearance within 12 d ($p < 0.001$). %age of NK cells in lungs were reduced ($p < 0.01$) in VLP vs. AP group with higher ($p < 0.001$) neutrophil proportions in response to infection with influenza virus in each group, respectively. The VLP group had less influenza NP-specific CD8+ T cells at days 8 ($p < 0.05$), 15 ($p < 0.05$), and 30 ($p = 0.001$). Switching VLP to AP diet improved CD4+ and CD8+ T cell subset levels on days 8 ($p < 0.01$), 15 ($p < 0.01$), and 30 ($p < 0.01$) and increased IFN- γ ($p < 0.001$).	[25]
3	Animal study (mice)	Mycobacteria-infected mice fed 2% protein diet vs. control group receiving 20% protein diet for up to 30 days.	100% of malnourished mice (fed 2% protein diet) succumbed to <i>M. tuberculosis</i> infection within 66 d.p.i. Malnourished mice had a reduced expression of IFN- γ , TNF- α , and iNOS in the lungs. A mortal infection of <i>M. tuberculosis</i> in malnourished animals was reversed upon re-feeding with the 20% protein diet	[26]
Lipids				

1	Animal study (mice)	Mice infected with H5N1 virus treated with omega-3 polyunsaturated fatty acid-derived lipid mediator protectin D1 (PD1), given 3 times i.v.	H5N1 virus pathogenicity decreased with higher levels of PD1. PD1 inhibited virus replication ($p < 0.001$) via influenza virus nucleoprotein mRNA expression at day 2 p.i. PD1 treatment within 12 h improved the survival ($p < 0.05$) and pathology of severe influenza ($p < 0.001$).	[27]
2	Animal study (mice)	Influenza A virus (IAV) infected mice fed with a high-fat (HF, 40% of energy) vs. low-fat (LF, 12% of energy) diet for 10 weeks.	HF mice were more susceptible to respiratory disease after IAV infection than were LF mice, with lower blood oxygen saturation ($p < 0.05$) and an increase in pulmonary viral load ($p < 0.05$). Decreased pro-inflammatory response to IAV in the serum of HF mice vs. LF for IL-6, IFN- γ , IFN- α , and IP-10 ($p < 0.05$). Antiviral response in the heart was reduced in HF mice after IAV infection, where higher viral loads were detected in the hearts of HF vs. LF mice ($p < 0.05$). Correlation between IAV-infected HF mice and viral infection in the heart, left ventricular mass, and thickening of the left ventricular wall, characterized by increased HIF-1 α compared to LF group ($p < 0.05$).	[28]
3	Animal study (mice)	High-fat diet (HFD) 60% or regular-fat diet (RFD) 5% fat, administered to 4-week old mice for 10 weeks. Influenza vaccination was conducted after 10 weeks.	Functionality of macrophages was diminished after diet-induced obesity ($p < 0.001$) via lower CD86-expressing macrophages, lower release of IL-6 and TNF- α , increased Th1 cell subpopulation, and reduced proportion of Treg cells. Vaccination-induced antibody production was decreased in animals receiving HFD vs. RFD ($p < 0.001$).	[29]
Lipids, carbo-hydrates				
	Animal study (mice)	Feeding mice with ketogenic, i.e., low carbohydrate diet (KD, 90% fat) vs. standard high-fat (60% fats, 20% lipids) diet (HFD) for 7 d before influenza A virus (IAV) infection.	KD protected mice from lethal IAV infection and disease ($p < 0.05$) compared to HFD-fed mice. KD resulted in an expansion of T-cells ($p < 0.001$), compared with the HFD group. KD-fed mice had better blood O ₂ saturation ($p < 0.001$). KD diet was significantly related to improved antiviral resistance ($p < 0.001$).	[30]
Fiber				
1	Prospective human cohort study	Prospective human cohort study	Consumption of dietary fiber correlated with lowered mortality from infectious and respiratory diseases. Per 10 g/d increase in dietary fiber, the multivariate RRs for infectious and respiratory diseases were 0.66 (CI: 0.52–0.84) and 0.82 (CI: 0.74–0.93) in men and 0.61 (CI: 0.44–0.85) and 0.66 (CI: 0.56–0.78) in women, respectively.	[31]
2	Animal study (mice)	High-fiber diet (HFD)-fed mice vs. control group, subjected to viral influenza infection	Intake of dietary fiber improved influenza by prolonged survival ($p < 0.05$) and ameliorated clinical scores ($p < 0.001$). After 7 d, HFD-fed mice with high-dose infection had better lung function as shown by reduced pulmonary resistance ($p > 0.01$) and enhanced compliance in response to methacholine ($p > 0.01$). In HFD-fed mice, the excessive neutrophil influx into the airways was inhibited	[32]

			by blunted levels of CXCL1, produced by lung monocytes and macrophages ($p < 0.001$) vs. controls. Increased antiviral immunity by dietary fiber through CD8+ T cell activation ($p < 0.01$) vs. controls. (HFD)-fed mice showed enhanced adaptive immunity by changed CD8+ T cell metabolism ($p < 0.05$).	
3	Animal study (mice)	Fiber-free diet group (LFD) vs. control group for up to 40 d, subjected to infection with mucosal pathogen <i>Citrobacter rodentium</i> .	Low fiber intake resulting in increases in mucus-degrading microbiota and enhanced lethal colitis cases ($p < 0.05$).	[33]
Vitamin A				
1	Meta-analysis of RCTs.	Effects of vitamin A supplementation on acute lower respiratory tract infections (LRTI). 10 studies ($n = 33,179$ children).	Though some individual studies demonstrated a positive effect of vitamin A supplementation on LRTI, in pooled Analyses, there was no effect of vitamin A supplementation on acute LRTI incidence or prevalence of symptoms.	[34]
2	Meta-analysis of RCTS	Assessment of vitamin A supplementation on acute respiratory infection. 5 studies ($n = 2177$ children (1067 children under intervention, 1110 control).	Faster recovery from infection symptoms due to vitamin A, no differences in the placebo group: fever: OR: 0.03, CI: $-0.10-0.17$; oxygen requirement: OR: -0.08 , CI: $-0.31-0.16$; increased respiratory rate: OR: -0.09 , CI: $-0.38-0.19$; hospital stay duration: OR: -0.06 , CI: $-0.52-0.40$.	[35]
Vitamin D				
1	Retrospective human study	Study determining mortality patterns of COVID-19 and associated factors: Special focus on vitamin D status. 2 cohorts of 780 cases with confirmed infection of SARS-CoV-2 in Indonesia	Vitamin D status is strongly associated with COVID-19 mortality (adjusted for age, sex, and comorbidity) ($p < 0.001$). Individuals with insufficient vitamin D status were ca. 12.6 as likely to die (OR 12.55).	[36]
2	Meta-analysis of RCTs	Assessment of vitamin D supplementation on respiratory tract infections. 5 clinical trials ($n = 964$ participants).	Significantly fewer respiratory tract infections were observed following a vitamin D supplementation. (OR: 0.58, CI: 0.417–0.812). In clinical trials there were beneficial effects on events of infections due to vitamin D supplementation in children (OR: 0.58, CI: 0.416–0.805) and adults (OR: 0.65, CI: 0.472–0.904).	[37]
3	Meta-analysis of RCTs	Assessment of vitamin D supplementation on respiratory tract infection (RTI). 11 placebo-controlled studies (RTCs) ($n = 5660$ patients).	Vitamin D had protective effects against RTI (OR: 0.64; CI, 0.49- 0.84). This was more pronounced by individual daily dosing compared to bolus doses (OR = 0.51 vs. OR = 0.86, $p = 0.01$).	[38]
Vitamin E				

Humans, RCT	Assessment of vitamin E supplementation and community acquired pneumonia. n = 7469 men 50–69 y.	Lower incidence of pneumonia in individuals receiving vitamin E supplements (RR: 0.28; CI: 0.11–0.69).	[39]
Vitamin C			
Meta-analysis of RCTs	Supplementation trials with vitamin C and observation of cold symptoms. 9 randomized controlled trials (n = 5500) in children (3 months–18 y of age).	Daily supplementation in vitamin C with extra doses reduced the time of having a common cold (mean difference = -0.56, 95% confidence interval (CI) (-1.03, -0.10)), fever (mean difference = -0.45, 95% CI (-0.78, -0.11)) and chest pain (mean difference = -0.40, 95% CI (-0.77, -0.03))	[40]
B-vitamins			
Human cross-sectional study	Observation of inflammation markers and nutrient status. HIV infected participants (n = 180 men, 134 women; 18–60 y)	Serum CRP concentrations were inversely associated with increased vitamin B intake including niacin, pyridoxine, and cobalamin (p for trend p < 0.01, p < 0.05 and p = 0.037, respectively) in men. Trends were observed in women.	[41]
Zinc			
Human double-blinded RCT	Patients in the zinc group (n = 50) received lozenges (13.3 mg of zinc gluconate) as long as they showed cold symptoms. Patients in the placebo group (n = 50) received 5% calcium lactate pent hydrate.	A faster decrease of the cold symptoms (median, 4.4 d vs. 7.6 d; p < 0.001), e.g., fewer days with coughing (median, 2 d compared with 4.5 d; p < 0.05), hoarseness (2 and 3 d; p < 0.05), headache (2 and 3 d; p < 0.05), nasal congestion (4 and 6 d; p < 0.01), and sore throat (1 and 3 d; p < 0.001) were found in the intervention group, supplemented with zinc, in comparison with the placebo group	[42]
Iron			
Animal trial (Wistar rats)	Administration of low iron diet (4–5 mg powder), medium iron diet (15 mg), control group (35 mg) and normal iron intake diet group. At week 4, rats received injection of inactivated porcine influenza vaccine (HswIN1).	Following immunization, anemic rats exhibited decreased (p < 0.05) antibody titer vs. controls. Antibody synthesis was preserved in moderate iron deficiency, but was hampered by severe anemia.	[43]
Selenium			
Human randomized, double-blinded RCT	Evaluation of response to influenza vaccine. 12-weeks follow up. n = 119 (50–64y) 6 intervention groups: 50, 100, or 200 mgSe/day, meals with Se-enriched onions (50	SEPS1 mRNA (marker of inflammation) increased (p < 0.05) after one week of vaccine administration, being dependent on the dose of Se per each intervention arm.	[44]

	mg se/day), unenriched onions and placebo.		
Polyphenols			
Animal study (mice)	Evaluation of effect of polyphenol extract from <i>Cistus Incanus</i> on avian influenza A virus (H7N7). Inbred female Balb/c and C57Bl/6 mice at the age of 6–8 weeks.	The polyphenol extract helped mice to not contract avian influenza, and to not alter bronchiole epithelial cells, as well as to keep constant the body temperature and the gross motor activity.	[45]
Carotenoids			
Carotenoids	Observation of β -carotene in plasma. 194 HIV-infected infants	β -Carotene was related to increased risk of death during HIV infection (OR: 3.16, CI: 1.38 to 7.21; $p < 0.01$)	[46]

Abbreviations: AP: adequate protein; Balb/c: albino mouse strain; CD-86: cluster of differentiation 86; CRP: C-reactive protein; CXCL1: The chemokine (C-X-C motif) ligand 1; H5N1- influenza A virus subtype H5N1; H7N7: influenza A virus subtype H7N7; HF: high fat; HFD: high-fat diet; HFD: high-fiber diet; HswIN1: swine influenza virus; IAV: influenza A virus; IFN- α/γ : interferon α/γ ; IL6: interleukin 6; LF: low-fat; LRTI: lower respiratory tract infections; iNOS: inducible nitric oxide synthase; KD: ketogenic diet; NK: natural killer cells; P1- protectin D1; RCT: randomized controlled trial; RFD: regular-fat diet; RTI: respiratory tract infection; SEPS1: selenoprotein S; TNF- α : Tumor necrosis factor alpha; VLP: very-low protein.

Methods of prevention

At present, no treatment for pneumonia caused by the new covid-19 virus. The vaccine development is still in the animal and some cases of disease testing phase, and suggestions and measures to control the spread of infection are still the only way to prevent the spread of the 2019-nCoV virus (covid-19). It should be noted that covid-19 infection is a new type of infectious disease, which is vulnerable to anyone. Legion ncov 2019 infection was legally classified as a category B infectious disease, but it was managed as a category A infectious disease. It is extremely important to implement infection control measures by Taking into account the quality of nutrition in addition to controlling the source of the infection, obstructing the transmission route and protecting the vulnerable population[47,48].

Conclusion

Despite the passage of nearly a full year since the emergence of the Corona pandemic (Covid-19) and despite its invasion of the whole world, but there is still a great deficit in discovering a cure for this disease so far, and even those that have been announced, still need more testing So it goes to the market, which makes the continuation of maintaining the diet to strengthen the immune system an urgent need, and it needs more research, testing and attention, especially patients with this disease, especially the elderly or those suffering from other diseases . Other preventive measures must be taken by avoiding unhealthy behaviors, adherence to social distancing, the use of disinfectants, and other measures aimed at preventing the spread of infection.

Summary

In summary, this review fully presents the phytonutrients that have been addressed in previous studies that have an effect on immunity and reduce the risk of infection, especially during the Covid-19 crisis, as the food components that we have referred to interact with the immune system and viral infection through a series of complex chemical reactions, confirming However, diet positively affects immune function.

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