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The relationship between serum vitamin D level and COVID-19; a review study



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Abstract

Introduction: Coronavirus disease 2019 (COVID-19) from the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is one of the most important epidemiological events in the past 100 years has become, the consequences for public health and economic systems around the world. Vitamin D is an important micronutrient that has been reported to improve immunity and protect against respiratory diseases. In this study, we intend to review articles that examine the relationship between COVID-19 and vitamin D. **Methods:** This is a review that uses articles from studies published in 2020 on the relationship between

Methods: This is a review that uses articles from studies published in 2020 on the relationship between COVID-19 and vitamin D in databases such as; Web of Science, Science Direct, SID, Magiran, Google Scholar and PubMed. Keywords used included; serum levels of 25-hydroxyvitamin D, vitamin D, COVID-19, SARS-COV-2 and coronavirus 2. With this search, 32 articles were finally selected for this purpose and their results were reviewed

Results: Of the 32 studies reviewed, only three showed no association between vitamin D levels in the blood and COVID-19 disease. Other studies had a relationship between the severity of the disease, mortality rate and length of hospital stay, in different age, gender and location groups.

Conclusion: It seems that the level of vitamin D in the blood has a potential effect on COVID-19 disease. Checking the serum vitamin D levels and supplementation in people with hypovitaminosis D can be a good solution to reduce the complications and problems caused by COVID-19.

Introduction

2019 (COVID-19) from Coronavirus the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is one of the most important epidemiological events in the past 100 years has become, with deleterious consequences for public health and economic systems around the world. COVID-19 infection can lead to a mild or very acute respiratory syndrome that is triggered by a change in the secretion of inflammatory cytokines (cytokine storm) which can be fatal in children, elderly populations, chronic lung patients or patients with high blood pressure and people who live in cities with air quality (1). Vitamin D is an important micronutrient and improves immunity and protects against respiratory diseases

Key point

Our review showed the level of vitamin D in the blood has a potential effect on COVID-19 disease. Checking the serum vitamin D levels and supplementation in people with hypovitaminosis D can be a good solution to reduce the complications and problems caused by COVID-19.

(2). Vitamin D is known for its activity in the respiratory system, and its deficiency is associated with pneumonia. It has been hypothesized that low levels of vitamin D may play a role in influenza virus infection. According to a recent meta-analysis of 25 trials (11321 participants), based on studies on different populations showed that vitamin D supplementation reduced the risk of acute respiratory infection (3). Through several

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mechanisms, vitamin D can reduce the risk of infection. These mechanisms include the induction cathelicidins and defensins, which can slow the replication of the virus and reduce the concentration of pro-inflammatory cytokines, which cause inflammation that damages the lining of the lungs and leads to pneumonia. It also increases the concentration of anti-inflammatory cytokines. Evidence for the role of vitamin D in reducing the risk of COVID-19 suggests that its prevalence occurred in winter, when 25-hydroxyvitamin D (25(OH)D) concentrations were lowest (4). Despite the difficulty of comparing data across countries, COVID-19 mortality is clearly higher in some countries than in others. Many factors may play a role, including differences in the proportion of older people in a population, the level of public health, access and quality of health care and socioeconomic status. The relative status of vitamin D in the population is often overlooked, which can affect the outcome of COVID-19. Because people are advised to stay home as long as possible, British government health agencies have advised people to take vitamin D supplements during an outbreak. Vitamin D supplementation can be very important for the elderly because they are at high risk for COVID-19 and vitamin D deficiency (5). COVID-19 is highly transmissible and can lead to acute lung damage in some patients. By balancing the activity of the renin-angiotensin system, the enzyme converter angiotensin 2, which is a receptor for fusion of the virus, has a protective role against the effects of this viral infection. Vitamin D can induce the expression of the angiotensin-converting enzyme and regulate the immune system through various mechanisms (6).

The main function of vitamin D is to retain calcium homeostasis and skeletal health. With a deficiency of this vitamin, only 10-15% of calcium and 60% of food phosphorus can be absorbed. While vitamin D supplementation enhancement calcium absorption to 30%-40% and phosphorus to 80%. Vitamin D is now known as a prohormone because it is synthesized in the body by the precursor of dehydrocholesterol under the influence of ultraviolet B (UB) rays with a wavelength of 290-315 nm in the skin, which is the main source of vitamin D. However season, latitude, time of day when the body is exposed to sunlight, skin color, age, use of sunscreen and type of coverage change the skin's synthesis capacity (7). Additional sources of vitamin D can be obtained through diet, including fish, eggs, leafy vegetables or fortified foods (8).

Serum levels of 25hydroxyvitamin D less than 20 ng/mL are called vitamin D deficiency. Vitamin D insufficiency is expressed with a serum level of 20-29 ng/mL and a normal state with a serum level of 30 ng/mL and above. It is necessary to mention the level of 30-50 ng/mL is defined as the ideal serum level of vitamin D (9).

Recently, the effects of vitamin D on SARS-CoV-2 infection, such as increased hospitalization and mortality, have been interested in scientific societies and in

universities. Numerous data, including known pathways of COVID-19, the physiology of vitamin D and its impact on the immune system, and population-based investigations and the association of vitamin D levels with respiratory infections, suggest that vitamin D deficiency is an important factor in the transmission of COVID-19 and the increase in its complications. Observational data comparing results from different populations show reverse relationship between vitamin D levels and the severity of COVID-19 and its mortality, suggesting a possible effect of vitamin D on the immune response to infection. In particular, Spain and Italy have high rates of vitamin D deficiency as well as some of the highest rates of COVID-19 infection and mortality worldwide. Conversely, Nordic countries have higher levels of vitamin D as a result of fortifying their diets with vitamin D with lower rates of infection and mortality of COVID-19. However, other data call such a link into question. Greece, for example, is one of the regions with the lowest prevalence and mortality of COVID-19 with a prevalence of vitamin D deficiency (25 (OH) D <20 ng/mL) of at least 50% over a wide age range. While Brazil, an equatorial country, has a high rate of COVID-19 deaths (10).

According to previous data that vitamin D can cause acute respiratory infections (ARI) prevent, it is natural to ask whether vitamin D can prevent COVID-19. Therefore, our goal is to review current articles in this field.

Materials and Methods

The present study is a review study in which articles related to studies published in 2020 related to the relationship between COVID-19 and vitamin D in databases such as; Magiran, Science Direct, SID, Google Scholar, and PubMed. Keywords used include; serum levels of 25hydroxyvitamin D, vitamin D, COVID-19, SARS-CoV-2, and coronavirus 2.

The criterion for selecting articles was the study of vitamin D levels in COVID-19 disease with case studies such as case study, cohort, clinical trial, series of cases, cross-sectional, observational. Exclusion criteria were lack of access to the full text of the articles and lack of quality conditions according to STROBE checklist. In addition, due to the outbreak of the disease on the last day of 2019, articles related to 2020 were extracted from databases. Finally, the comparable characteristics of the articles (including study location, study population, number of people studied, type of study and related results) were reported in Table 1.

Results

At first, 309 articles were found, after reviewing the title and removing irrelevant and duplicate titles, 173 articles were deleted and 136 articles were selected to review the abstract (Figure 1).

After reviewing the abstract (or in articles without abstracts after reviewing the original text), 104 unrelated

Table 1. Studies in association with vitamin D levels with COVID-19

Author Name	Location	Population	Number of people surveyed	Type of study	Result
D'Avolio et al (11)	Canton of Tessin, Switzerland	Adult Mean age 73 years	107	Retrospective March 1 to April 14, 2020	 When classifying patients in terms of age (0 to 70 years and >70 years) and positive PCR, vitamin D concentration There was no significant difference between the two groups. Vitamin D concentrations vary significantly when considering patients >70 years of age. This difference was not observed in patients under 70 years of age. There was a statistically significant difference in vitamin D concentration when dividing the group based on gender and PCR result.
MacLaughlin et al (12)	Chicago	People who took the COVID-19 test from March 3 to April 10, 2020	4314	Retrospective cohort	In this single-center retrospective cohort study, vitamin D deficiency was likely associated with an increased risk of COVID-19.
Kaufman et al (13)	50 US states	Patients tested mid-March to mid-June, 2020 Median age, 54 years	191779	Retrospective, observational	SARS-CoV-2 was more positive in patients with "low" 25 (OH) D than in patients with "sufficient" vitamin D. SARS-CoV-2 positivity is inversely related to circulating 25 (OH) D levels, a relationship that exists across latitudes, races/ethnicities, different genders, and age groups.
Ali (14)	20 European countries	Adult	Number of COVID-19 cases and deaths per million	Retrospective (From May 20, 2020)	A significant negative correlation between the mean levels of vitamin D and COVID-19 in every million people in the European countries is observed. However, the relationship between vitamin D and deaths from COVID-19 in these countries was not significant
Tan et al (15)	Singapore (a university hospital)	COVID-19 patients ≥50 year of age	43	Observational cohort (January 15 - April 15, 2020)	A combination of vitamin D/magnesium/vitamin B ₁₂ in older COVID-19 patients was associated with a significant reduction in the proportion of patients with clinical exacerbations who required oxygen support, intensive care support, or both.
Alipio (16)	Three hospitals in South Asia	COVID-19 patients	212 case	Retrospective multicenter study	The difference in mean levels of vitamin D in mild, natural and severe COVID-19 was remarkable. Low vitamin D levels are significantly associated with worse clinical outcomes
Lau et al (17)	United States of America (a first-class university medical center)	Adults Mean age 65.2 years	20	A retrospective observational study (March 27 - April 21, 2020)	Vitamin D deficiency was detected in ICU individuals (84.6%) compared to floor patients (57.1%)
Glicio et al (18)	Two tertiary medical centers in South Asia	Elderly over 60 years	176	Retrospective study	Majority of COVID-19 classified as severe had 25-hydroxyvitamin D3 level below 30 ng/mL. Age and 25(OH)D level were negatively related.
Hastie et al (19)	UK (Biobank UK 2006- 2010 data for vitamin D and ethnicity)	Adults 37 to 73 years	449	Cross-sectional (March 16 - April 14, 2020)	Vitamin D was similarly associated with COVID-19 infection, but no correlation was observed after adjusting for confounding variables. Adjustment for 25 (OH) D concentrations made little difference in correlation. Our findings do not support a potential link between vitamin D concentrations and the risk of COVID-19 infection, nor does vitamin D concentrations explain ethnic differences in COVID-19 infection.

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Table 1. Continued

Author Name	Location	Population	Number of people surveyed	Type of study	Result
Darling et al (20)	UK (Biobank UK 2006–2010 data for BMI, Vitamin D and ethnicity)	Adults Mean age 57.7 years	COVID-19 patient (n 580) and controls (n 723)	Retrospective	There was no significant difference in 25-hydroxyvitamin D3 levels between COVID-19 patient and the control group. 25-hydroxyvitamin D3 status was remarkably lower in Asian people, black skin and mixed ethnicities compared to white. Vitamin D levels were significantly lower in obese individuals.
Li et al (21)	Mainland of USA (48 states and Columbia district)	-	1 609 488 cases and 91094 deaths	Retrospective (January 22 to May 23, 2020)	Latitudes were marginally associated with cases and deaths Sunlight and vitamin D, with latitude as an indicator, possibly associated with reduced risks for both COVID-19 cases and mortality Latitude was relatively associated with cases and mortality. Sunlight and vitamin D, with the Latitude as a marker, possibly by reducing the risks to the COVID-19 and the associated mortality.
De Smet et al (22)	Belgium (Central Network Hospital)	Adults	186 cases and 2717 controls	Retrospective observations (March 1 - April 7, 2020)	COVID-19 patients showed lower levels of vitamin D deficiency. Surprisingly, this difference was limited to male COVID-19 patients who had significantly more deficiency than the male control group, which increased with advancing radiology
Daneshkhah et al (23)	Hospitals and clinics from different parts of the world	Patients under 80 years	5000 cases	As of March 21, 2020	Approximately 15% reduction in the number of critically ill COVID-19 patients who have a normal vitamin D status in a population
Raharusun et al (24)	Indonesia (Government Hospital)	Adults Mean age 54.5 years	780 case	Retrospective cohort study (March 2, April 2 to April 24, 2020)	In univariate analysis, elderly male patients with previous medical conditions and lower than normal vitamin D were accompanying with a higher probability of death. Vitamin D levels after adjustment of confounders (age, sex and co-morbidity) showed a strong association with COVID-19-induced mortality
Ling et al (25)	Three UK hospitals	Patients over 18 years of age		Retrospective cross-sectional observations 27 January 2020 to 5 August 2020	It seems that treatment with vitamin D, regardless of baseline serum vitamin D with reduced risk of death in patients hospitalized in Covid-19 is acute.
Fasano et al (26)	A great center in Lombardy, Italy	Parkinson's patients "case" their family "control"	1486 cases 1207 control	Case-control	COVID-19 risk and mortality did not differ from the general population, but it seems the symptoms are milder
Ohaegbulam et al (27)	New York	4 patients with vitamin D deficiency who were diagnosed with COVID-19 in April 2020	4	Series of clinical cases	Patients receiving high doses of vitamin D supplements return to normal levels of vitamin D and promote clinical improvement, which is evident with shorter hospital stays, less oxygen requirements, and reduced inflammatory markers. Vitamin D supplementation may be a good option for reducing acute respiratory distress syndrome in patients in low-income communities where sources of expensive and high-cost drugs may be scarce.

Table 1. Continued

Author Name	Location	Population	Number of people surveyed	Type of study	Result
Carpagnano et al (28)	Policlinic of Bari, Italy	42 patients who were diagnosed with acute respiratory failure due to COVID-19	42	Retrospective, observational study from March, 11 to April 30, 2020	A high prevalence of hypovitaminosis D was observed in COVID-19 patients with acute respiratory failure treated with RICU. Patients with severe vitamin D deficiency had a significantly higher risk of mortality. Severe vitamin D deficiency may be a sign of poor prognosis in these patients, suggesting that adjuvant therapy may improve disease outcomes.
Maghbooli et al (29)	Sina Hospital, Tehran, Iran	235 patients with COVID-19	235	Cross-sectional analysis of a COVID-19 database	A significant decrease in serum CRP, an inflammatory marker, along with the increase percentage of lymphocytes suggests that vitamin D sufficiency may also reduce the risk of a storm of cytokines in response to viral infection, to help dampen the immune response.
Baktash et al (30)	Wexham Park Hospital, United Kingdom	Patients aged ≥65 years presenting with symptoms consistent with COVID-19	105 people (70 people COVID-19 positive and 35 people COVID-19 negative)	Prospective cohort study between 1 March and 30 April 2020	COVID -19-positive arm demonstrated lower median serum compared with COVID-19-negative arm. No increased mortality was observed between groups. Older adults with vitamin D deficiency and COVID-19 may demonstrate worse morbidity outcomes.
Hars et al (31)	Hospital in the Caucasus	Older COVID-19 patients hospitalized mean age of 85.9 years	160 (95 females and 65 males)	Retrospective cohort (between March and April 2020)	Among affected patients, 34% of women and 42% of men were deficient in vitamin D (i.e., 25 [OH] D <50 nmol/L), with no significant sex difference. Severe vitamin D deficiency was independently associated with an in-hospital mortality risk in men. No association was observed in women
Panagioto et al ., u(32)	United Kingdom (Local Clinical Care Path)	134 patients with COVID -19	134	Retrospective interim audit	A higher prevalence of vitamin D deficiency was observed in patients requiring ITU admission compared to patients in medical wards.
Merzon et al (33)	Israel (Lumit Health Services)	People who have been tested for COVID-19 and have had a vitamin D test	7807 individuals 7025 COVID-19 negative and 782 COVID-19 positive	Population-based study From February 1 to April 30, 2020	Mean plasma vitamin D levels were significantly lower among those who tested positive for COVID-19 than those who tested negative. Univariate analysis showed an association between low plasma 25 (OH) D levels and an increased risk of COVID-19 infection and hospitalization due to SARS-CoV-2 virus.
Annweiler et al (34)	French nursing-home	COVID-19 positive cases	66	Quasi-experimental study	Vitamin D3 supplementation during or just before COVID-19 was associated with lower COVID-19 intensity and better survival in debilitated elderly
Arvinte et al (35)	North Suburban Medical Center, Thornton, Colorado	Critical COVID-19 patients admitted in May 2020	21 people (including 15 men and 6 women, including 17 Hispanics and 4 Caucasians, with median age 61)	A Pilot Study	This pilot study showed that vitamin C and vitamin D levels were low in most ICU cases with COVID-19 Many were also resistant to insulin or diabetes, overweight or obesity, which are known to be independent risk factors for low levels of vitamin C, vitamin D and COVID-19.

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Table 1. Continued

Author Name	Location	Population	Number of people surveyed	Type of study	Result
Abrishami et al (36)	Tehran University Hospital, Iran	COVID-19 positive cases	73 (mean age 55.18 and 46.4% male)	Retrospective study	The mean concentration of vitamin D serum in the deceased was significantly lower Higher levels of vitamin D were associated with significantly lower levels of lung involvement Vitamin D deficiency [25 (OH) D <25 ng/mL] was correlated with a significant increase in death risk
Radujkovic et al (37)	Hospital of Heidelberg University of Medical Sciences, Germany	COVID-19 positive cases	185	Prospective	Our study demonstrates the association between serum vitamin D deficiency and the severity or mortality of COVID-19, and highlights the need for intervention studies on vitamin D supplementation in people infected with SARS-CoV-2.
Ye et al (38)	Guangxi People's Hospital, China	80 controls and 62 patients with COVID-19	142	A Case-Control Study	Severe cases of COVID-19 were significantly older than mild cases and had a higher incidence of comorbidity (renal failure). Serum vitamin D concentrations in COVID-19 patients were much lower than in healthy individuals. And vitamin D levels were lower in severe cases than in mild cases
Karonova et al (39)	Russia	Patients with COVID-19 with a mean age of 53.2	80 people (43 men)	-	It was found that in patients with severe course, the level of 25(OH)D blood was significantly and vitamin D deficiency was more common than in patients with moderate to severe course of the disease The same pattern was revealed in patients with a fatal outcome, where the level of vitamin D was 10.8 \pm 6.1 ng/mL, compared with this indicator in patients discharged from the hospital (17.8 \pm 13.4 ng/mL)
Yılmaz et al (40)	Dicle University Faculty of Medicine	85 children from 1 month to 18 years	85 (40 cases with COVID-19 and 45 controls)	A Case-Control Study	Patients with COVID-19 had significantly lower levels of vitamin D than controls. Symptoms of fever were significantly higher in patients with COVID-19 who had low and insufficient vitamin D levels than in patients with adequate vitamin D levels.
Gonçalves et al (41)	Sao Paulo, Brazil	Elderly patients with a mean age of 72.9 admitted to the ICU	176 (54 % Male)	Cross-sectional descriptive study	Hypovitaminosis D and obesity are more common in older people admitted to the ICU due to severe coronavirus infection.
Tomisti et al (42)	Hospitals in Massa, Italy	Patients with COVID-19 pneumonia and non- COVID-19-related pneumonia and patients with acute non-respiratory disease	156 (3 groups of 52 people including 52 cases and 104 controls)	Retrospective Case-control Study	No differences in serum vitamin D levels were observed between the three groups. In the COVID-19 group, serum vitamin D levels did not show a significant relationship with mortality risk, intensive care unit admission risk, length of hospital stay, and recovery.

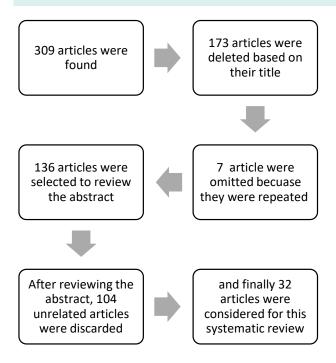


Figure 1. Flowchart steps for entering studies in a review

articles were discarded and finally 32 articles were considered suitable for this purpose and were reviewed and finalized. Additionally, some references to the mentioned articles that seemed to be relevant to the subject of the study were examined.

Of the 32 studies reviewed, only three showed no correlation between vitamin D levels in the blood and COVID-19 disease. Other studies had a relationship between the intensity of the disease, mortality rate, length of hospital stay, in different age, gender, location, etc groups.

Discussion

The present study was a systematic review of published studies on the relationship between vitamin D levels and SARS-CoV-2. According to published studies, the effect of serum vitamin D concentration on COVID-19 was observed. Although most of the studies showed a significant relationship between vitamin D levels and COVID-19, however it is possible to publish studies with more positive results, the publication bias is not far from expectation and this can be one of the limitations of this study. Another limitation could be the new and unknown disease and the lack of sufficient studies in this field.

The main findings of our study show that most patients with lower than normal serum vitamin D concentrations have complications more severe than in patients with adequate vitamin D levels. Possible cause for this observation can be explained by the role of vitamin D in a variety of immune responses.

Through several mechanisms, vitamin D can reduce the risk of infection. Understanding these mechanisms

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can logically indicate that patients with 25 (OH) D deficiency are at greater risk for more severe SARS-CoV-2 manifestations or a worse prognosis. Such as the behavior of seasonal viral respiratory tract infections, the distribution of SARS-CoV-2 prevalence in the community also shows seasonal patterns along latitude, specific temperature and humidity. Without considering age, ethnicity, and latitude, recent data show that 40% of People in Europe with a high prevalence of SARS-CoV-2 are deficient in vitamin D, and 13% are severely deficient in vitamin D (43).

In a study to survey the association between latitude and SARS-CoV-2 mortality, 88 countries were selected based on the possibility of providing reliable information. With using the mortality rate per million for each country from the "worldometers" website, a correlation analysis was performed among the mortality rate and the latitude of these countries. There was a positive and significant relationship between the lower mortality rates with the neighborhood of a country with the equator, which means that 16% of changes in mortality rates among countries are calculated in terms of latitude. Evidence has been provided that there is a clear link between sun exposure and reduced mortality. This survey demonstrates for the first time a statistically significant relationship between a country's latitude and its SARS-CoV-2 mortality and is consistent with other studies on latitude, vitamin D deficiency and SARS-CoV-2 mortality (44).

In another systematic review and meta-analysis study that was performed to investigate whether vitamin D deficiency exacerbates SARS-CoV-2, limited evidence of the effect of vitamin D in people with COVID-19 was found. In this study, the relationship between vitamin D deficiency and the severity of SARS-CoV-2 was analyzed by analyzing the prevalence of vitamin D deficiency and insufficiency in patients with this disease. The result was that vitamin D deficiency was not more likely to be associated with SARS-CoV-2 but was associated with severe cases of SARS-CoV-2. Serum vitamin D deficiency was also positively associated with hospitalization and COVID-19 mortality (45).

Another systematic and meta-analysis of the role of vitamin D in COVID-19 was performed. Around 16 studies with a total of 4922 participants were included in the meta-analysis. Meta-analysis showed that 48% of COVID-19 patients suffered from vitamin D deficiency and in 41% of patients the vitamin D level was insufficient. Serum vitamin D concentration among SARS-CoV-2 patients was 18 ng/mL. 47.4% of them have hypertension, 32.1% diabetes, 30.4% cardiovascular disease, 27.1% chronic kidney disease, 22.0% obesity, 17.5% respiratory disease, 14.5% depression/anxiety, 7.4% cancer and 5.1% dementia in addition to COVID-19 and the ethnic groups participating in this study were 1.0% Caribbean African, 10.3% Asian and 92.1% Caucasian. This survey showed that the mean serum level of 25-hydroxyvitamin D was low in all SARS-CoV-2 patients and most of them suffered

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from vitamin D deficiency. Most participants were Caucasian, and the highest comorbidity with COVID-19 was in patients with hypertension, diabetes, cardiovascular disease, chronic kidney disease, obesity, and respiratory disease, which may be directly or indirectly affected by vitamin D deficiency (46).

In another survey, a second-class relation was found between the prevalence of vitamin D deficiency in most commonly affected countries by SARS-CoV-2 and the latitudes. Vitamin D deficiency is more common in the subtropical and mid-latitude countries than the tropical and high-latitude countries. The most commonly affected countries with severe vitamin D deficiency are from the subtropical (Saudi Arabia 46 %; Qatar 46 %; Iran 33·4 %; Chile 26·4 %) and mid-latitude (France 27·3 %; Portugal 21·2 % and Austria 19·3 %) regions. Severe vitamin D deficiency was found to be nearly 0 % in some high-latitude countries (e.g. Norway, Finland, Sweden, Denmark and Netherlands) (43).

Although the protective effect of vitamin D against COVID-19 is still not completely valid, there are reasons why it is recommended to maintain normal levels of vitamin D in the blood, especially in this epidemic, in conditions of social isolation and winter to prevent severe deficiency. In addition to the specific effects of vitamin D on respiratory function, vitamin D supplementation is usually recommended for the general public because of its obvious benefits to the musculoskeletal system.

The recommended doses of vitamin D vary from 400 to 2000 IU per day depending on age groups and clinical conditions. These doses are sufficient to prevent severe deficiency and are very safe without the risk of poisoning.

Conclusion and recommendations

This systematic review has shown that having optimal levels of vitamin D in individuals can play a protective role against respiratory infections, especially infections caused by COVID-19.

Therefore, people who are exposed to vitamin D deficiency should try to increase their serum vitamin D levels by using proper nutrition, exposure to sunlight at the right time, and taking vitamin D supplements, therefore they may be safe from COVID-19

Authors' contribution

YK, MSM, AS and SH, all were participated in drafting preparing the paper and statistical analysis of the paper. MSM is a corresponding author and conducted the final check and manuscript edit. All authors read and signed the final paper.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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