

The Covid-19 Disaster

And what should have been done by the WHO and other world health authorities, and will still be profoundly useful.

Information compiled by Professor Ian Brighthope

In addition to the recommendations in place regarding the prevention of the spread of Covid19, some simple and inexpensive measures could have been put in place and possibly saved human lives and the economic tragedies that have befallen the global population.

The Covid19 virus is a member of the common cold group of viruses. It has undergone genetic changes and become highly virulent and deadly to some, especially the aged and those with weakened immune systems.

We know from the medical and scientific literature that optimal nutrition is one of the main factors for a healthy well functioning immune system. Both vitamin C (ascorbic acid) and vitamin D are essential to and effective in supporting and strengthening the immune system.

Vitamin C also has antiviral activities against many viruses including the common cold and the influenza viruses.

Vitamin C at 1000-4000 mg per day will reduce the severity and shorten the duration of the common cold. Increasing the dose to 10,000 mg per day is required for more severe colds and in cases of mild to moderate influenza.

Much larger doses are required for those moderately to seriously ill with the Covid19 virus, especially if the patient is deteriorating. Doses of 100,000 mg and more have been given to seriously ill patients with, for example, viral pneumonia. These doses must be given intravenously. Please see the references below and the two 60 Minutes shows.

These dosing schedules are no different to the use of antibiotics for bacterial infections. A throat infection can be treated with low dose oral antibiotics. A lung infection will require much higher doses and if serious pneumonia occurs, IV injections.

There are physicians in most countries who have been giving these high doses of vitamin C for many decades. Hundreds of thousands of patients have benefited from intravenous vitamin C. Vitamin C is recognised as a

valid treatment by specifically and highly trained doctors in the medical profession.

Another vitamin, vitamin D, has been proven to protect people against many viruses including the influenza viruses and the corona viruses. This protection extends to significantly reducing the risks of serious viral pneumonia and death.

An article from the British Medical Journal in 2017 (BMJ 2017;356:i6583) titled “Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data” concluded that:

‘Vitamin D supplementation was safe and it protected against acute respiratory tract infection overall. Patients who were very vitamin D deficient and those not receiving bolus doses experienced the most benefit.’

The issue with vitamin D is that we don’t know the blood levels of vitamin D in the general population. We do know that intakes are low, exposure to sunlight is inadequate, and the elderly and those in institutions are often very deficient.

Have we forgotten that our grandparents gave us cod liver oil in the winter.

The reason, to ward off the effects of the common cold. How did it work? It contained vitamins A and D.

The cost to supplement an adult with 1000-2000 International Units of vitamin D per day is 7-14 cents at current retail prices. This equates to about \$25-\$50 a year. Compare this cost to the economic tragedy and loss of lives from influenza and now the Corona virus.

Nutrients are powerful therapeutic agents. Without vitamins we die. With inadequate vitamin levels we get sick. With optimum levels, we thrive and reduce the risk of disease and death.

When are the authorities going to wake up? After the next round of deadly flu, SARS, MERS and Swine?Bird flu.

My family, friends, relatives and intelligent colleagues will be supplementing.

Ian Brighthope

11 March, 2020

Here are the DropBox Links to two 60 Minute TV shows on the use of High dose Intravenous Vitamin C. Essential Viewing for those who want to Understand the Power of Nutrients in Saving Lives.

https://www.dropbox.com/sh/qz2vnniv1g45zpe/AACxIJc_xV6mvLVcW-S2qD5oa?dl=0

Intravenous ascorbate in the treatment of influenza: lack of evidence or incontrovertible ignorance?

Professor Ian Brighthope

“Are we to retreat from human experience into the desiccation of laboratory jargon in order to achieve respectability. I think not! Human ailments should somewhere relate to human beings. And if a properly observed and recorded instance of patient disease reaches the press it may very well be worth reams of laboratory data.”

—Wilfred E. Wooldridge, M.D. *In defense of the anecdotal article*

The sixty-minutes documentary ‘Living Proof’ aired on New Zealand television in 2010 told

the miraculous story of N.Z. King Country dairy farmer Alan Smith, who after contracting the H1N1 virus (Swine Flu) was admitted to intensive care with bilateral pneumonia, renal failure and leukaemia. He was eventually placed on life support. His condition deteriorated. With his lungs unable to function, and with no hope of their patient making a recovery, it was determined by his attending doctors that the ‘ECMO’ equipment [*Extra Corporeal Membrane Oxygenation*] artificially sustaining Mr Smith be switched off. Not satisfied with this position, Alan Smith’s family rallied, and despite reluctance by the hospital authorities, they insisted that he be administered high dose intravenous ascorbic acid (vitamin C).

After much heated debate and consultation the hospital staff eventually agreed to the family's request and began to administer the intravenous ascorbic acid to Mr Smith, at 100g per day. He recovered to the point where his lung function returned and he was taken off the ECMO life support. The treatment was then mysteriously withdrawn. The family insisted it be re-instigated. The hospital resisted. The family brought in a medical lawyer. The hospital relented but the doses they administered were less than optimal. Fortunately the treatment worked and Alan Smith is now alive and well over 12 months later, and without any sign of his leukaemia.

Where's the evidence?

According to Alan Smith, "in a nut shell I would not have survived if I hadn't had the Vitamin C." Unfortunately the medical 'authorities' in Zealand were not so convinced. In a recent statement released by the *Auckland District Health Board*, Dr Margaret Wilsher denied that there was sufficient evidence to confidently say that high-dose vitamin C therapy is either safe or effective.

This is at odds with the basic science and the clinical science, which are available through the major medical databases. Since it's discovery in the 1930's it should be noted that many thousands of papers have been published in the medical literature supporting the use of vitamin C.[1] Some of the conditions studied with positive clinical outcomes include reducing the risk of heart disease, slowing the progression of atherosclerosis, cataract prevention, preventing asthma attacks, blood pressure reduction and the list goes on . . . [2] [3] [4] [5] [6] Many of these studies were conducted

using oral doses rather than intravenous doses, nevertheless this research is still noteworthy, and as I will discuss later in this article, sometimes both oral and IV administration are required.

Whilst there are few recent studies to support the use of IV ascorbate in the treatment of influenza and other viral infections, the evidence does exist. Landmark studies published by Dr Frederick Klenner as early as 1949 demonstrated the potential of intravenous ascorbate for the inhibition of virus replication and the virtual elimination of viral illnesses such as hepatitis, poliomyelitis and influenza [7] The scientific genius Linus Pauling, who famously championed the use of high doses of vitamin C,

was well aware of the potential of ascorbic acid as a preventive measure in viral infections such as influenza. [8]

He suggested that at the onset of infection taking 1g (1000mg) per hour would usually defeat the virus. [9] Until recently the mechanism of action was uncertain, although there is quite recent in vitro evidence (2008) that confirms the direct anti-viral activity of both ascorbic acid and dehydroascorbic acid (ascorbic acid in its reduced form) in defined conditions. [10]

From my personal clinical experience Vitamin C is well established as a potent antiviral, it is also antibacterial, antifungal, anti-rheumatoid cell, antimelanoma cell, antileukaemia cell and it can achieve these effects at levels achieved by the IVC route. Vitamin C also stimulates the immune system by increasing complement, modulating inflammatory mediators and increasing the number and activity of helper cells and killer cells.

In 1995, Riordan published data demonstrating that sustained plasma levels of ascorbic acid in humans are toxic to tumor cells. These levels could only be attained by the intravenous administration of this therapy. [11] [12] [13] This beneficial activity of ascorbate was confirmed in subsequent vitro tests conducted by the National Academy of Sciences in 2005. [14]

Ascorbic acid also has many biochemical functions including stress hormone support and its most celebrated quality is its antioxidant capabilities. Vitamin C is the safest, most powerful and ubiquitous free radical scavenger (antioxidant) known to biology and it can very quickly remove free radicals such as superoxide, nitric oxide, hydroxyl, lipoperoxides and peroxynitrates from organs and tissues.

These radicals are formed as a consequence of severe infection, trauma, oxygen treatment, intravenous medical drugs, surgery and stress, most of these being issues within intensive care units. Fulminating infections and white out pneumonia as in the swine flu cases occur essentially because the biological system has been completely exhausted of its capability of capturing, sinking, mopping up and neutralising these radicals and impaired rogue electrons

Vitamin C: A misnomer

Ascorbic acid used therapeutically at pharmacological doses via intravenous infusion is a distinct entity from what we know as dietary ‘vitamin C.’ As Ely observes, “*the popular view that ascorbic acid is a vitamin is mistaken. This mistake is a major cause of massive tragic unnecessary morbidity and mortality, rapid aging, and shortened life spans.*” [1]

In the clinical context intravenous ascorbic acid is a pharmacological agent and not a simple nutrient or vitamin required in daily doses which conform to the desired targets (Recommended

Daily Intake, Recommended Daily Allowance, Adequate intake levels etc) set out by the World Health Organization and other government agencies. Whilst an acceptable daily intake of dietary vitamin C would certainly help delay or prevent the onset of infection from viruses such as the H1N1 strain, once someone has been infected by the virus and is presenting with serious symptoms, we need to call in the cavalry, so to speak. Much higher doses to the point of tissue saturation are required.

In the words of Frederick R. Klenner, M.D., “*Its neutralizing action on certain toxins, exotoxins, virus infections, endotoxins and histamine is in direct proportion to the amount of the lethal factor involved and the amount of ascorbate given. At times it is necessary to use ascorbate intramuscularly. It should always be used orally, when possible, along with the needle.*” [15]

In the late 1970’s I established a clinic for the specific use of IVC. Large numbers of very sick patients with virtually any condition were given between 15 and 60/grams of ascorbic acid by IV injection. Without doubt, most patients responded positively, including patients with cancer, AIDS and many other serious conditions. Some of the most dramatic responses in which nothing else could be done medically were in the treatment of patients with viral illnesses. There was a notable case, a 21-year -old young woman suffering from the most severe case of adult chicken pox.

The lesions in her throat and trachea made it impossible for her to swallow, and also made it difficult and painful for her to breathe. She felt better within an hour of receiving 30/grams of IVC. She had two more injections, which stopped the development of any further lesions. Adult chicken pox can cause a fatal pneumonia — yet this girl didn’t even need to be admitted to hospital after receiving IVC. Similar instances were observed

with Herpes simplex, zoster and many other viruses. The most common ailments presenting on a daily basis were respiratory viral infections — not so much the common cold but influenza and infectious mononucleosis.

Intravenous administration by Nurses in pharmacy

The authorities and experts are warning us that a killer flu pandemic is inevitable. Whilst we have vaccines and antiviral drugs that we can stockpile for such an occurrence, doubt remains as to their effectiveness. To meet a challenge in which the drugs and vaccines are only partially effective, I contend that the widespread use of IVC in moderate to severe cases of influenza be made available. In the case of a pandemic, there is not the medical manpower available to treat large numbers of moderately to severely ill influenza patients. Thus, I propose the training of nurses in the proper administration of IVC, and these nurses be located in community pharmacies (and GP clinics if the GP is willing to participate), making this safe, effective and inexpensive treatment option available to all. From my experience, it has the potential to save many lives — and its safe and inexpensive

The sad conclusion

As a result of the sixty minutes documentary on the miraculous recovery of Alan Smith, I was recently approached by a man in Australia asking about the use of intravenous vitamin C.

As this man explained his 20 year old sister was in a coma on ECMO life support and in critical care and he was keen to approach the hospital about using IV ascorbic acid. The young woman's family had seen the 60 Minutes story and set about tracking down Allan Smith in New Zealand. The hospital agreed reluctantly to administer 60 grams per day of IV ascorbate. The patient improved considerably. Her lungs cleared and regained functionality and she was taken off the ECMO

machine. Then despite my warnings they then discontinued the treatment. Her condition deteriorated and eventually she died from pancreatitis and liver failure.

Afterword

It is time that the medical orthodoxy embraced the use of intravenous Vitamin C to save lives and improve prognoses. Patients are dying as a result of the failure of our medical system to use IVC. As researcher Mark

Levine has observed, after fifty years of study and debate, the use of intravenous ascorbic acid remains ‘controversial, colourful and emotional,’ it being forced into ‘*culs de sac, regressions and periods of blindness and amnesia*’ by its opponents. [16]

As one such opponent, Dr David Ghaller, a senior intensive care specialist in New Zealand has stated, “we as a group believe it is harmful, and in this setting of critical illness, potential for harm outweighs any therapeutic benefit.” In light of the actual evidence, anecdotal or otherwise, such a statement beggars belief. It doesn’t work because they haven’t tried it. It doesn’t work because they have been told it doesn’t work, it is a major myth in the medical profession that needs to be debunked once and for all.

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Here are the DropBox Links to two 60 Minute TV shows on the use of High dose Intravenous Vitamin C.

Essential Viewing for those who want to Understand the Power of Nutrients in Saving Lives.

https://www.dropbox.com/sh/qz2vnniv1g45zpe/AACxIJc_xV6mvLVcW-S2qD5oa?dl=0

[Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data](#)

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BMJ 2017; 356: i6583 (Published 15 Feb 2017)

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Research News

[Vitamin D supplementation does cut respiratory infections, new study suggests](#)

Gareth Iacobucci

BMJ 2017; 356: j847 (Published 16 Feb 2017)

...Gareth Iacobucci The BMJ The debate over whether patients should be encouraged to supplement their diet has reignited after a study found that vitamin D supplementation can help reduce the risk of acute respiratory tract infections. Researchers from Queen Mary University of London argued ...

[PDF](#) [Research News](#)

[Vitamin D supplementation does cut respiratory infections, new study suggests](#)

[Gareth Iacobucci](#)

From the British Medical Journal:

BMJ 2017;356:i6583

Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data

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Additional material is published online only. To view please visit the journal online.

cite this as: *BMJ* 2017;356:i6583 <http://dx.doi.org/10.1136/bmj.i6583>

Accepted: 01 December 2016

ABSTRACT

Objectives

To assess the overall effect of vitamin D supplementation on risk of acute respiratory tract infection, and to identify factors modifying this effect.

Design

Systematic review and meta-analysis of individual participant data (IPD) from randomised controlled trials.

Data Sources

Medline, Embase, the Cochrane Central Register of Controlled Trials, Web of Science, ClinicalTrials.gov, and the International Standard Randomised Controlled



RESEARCH NEWS

Vitamin D supplementation does cut respiratory infections, new study suggests

Gareth Iacobucci

The BMJ

The debate over whether patients should be encouraged to supplement their diet has reignited after a study found that vitamin D supplementation can help reduce the risk of acute respiratory tract infections.

Researchers from Queen Mary University of London argued that their findings, published in *The BMJ*,¹ support the introduction of food fortification in the UK.

But in a linked editorial other academics, who recently questioned the evidence using vitamin D supplements to prevent disease, said that a clinically useful effect remains uncertain and requires confirmation in further “well designed, adequately powered” randomised controlled trials.²

After setting out to determine the overall effect of vitamin D supplements on the risk of acute respiratory tract infection the researchers conducted a systematic review and meta-analysis of individual participant data from 25 randomised controlled trials of vitamin D supplementation, involving 11 321 participants aged 0 to 95.

The study, which was adjusted for age, sex, and study duration, found that vitamin D supplementation resulted in a 12% reduction in the proportion of participants experiencing at least one acute respiratory tract infection (adjusted odds ratio 0.88 (95% confidence interval 0.81 to 0.96)).

The researchers calculated that 33 people would need to take vitamin D supplements to prevent one acute respiratory tract infection. The benefit was greater in people receiving daily or weekly vitamin D without additional large (bolus) doses (0.81 (0.97 to 0.86)).

The protective effects in people receiving daily or weekly vitamin D were strongest in those with severe deficiency (<25 nmol/L baseline blood levels) (0.30 (0.17 to 0.53)). The researchers calculated that only four people in this group would need to take supplements to prevent one acute respiratory tract infection.

The study also showed that use of vitamin D was safe, the authors said, as potential adverse reactions were rare.

They acknowledged some limitations of the study, including limited power to detect the effects of vitamin D in some groups. But they concluded, “Our results add to the body of evidence supporting the introduction of public health measures such as food fortification to improve vitamin D status, particularly in settings where profound vitamin D deficiency is common.”

In an editorial Mark Bolland, from the University of Auckland in New Zealand, and Alison Avenell, from the University of Aberdeen, UK, argued that the absolute risk reduction of 2% found in the study would not be a sufficient justification for most of the general population to take supplements. They said that the results should be viewed as “hypothesis generating only” and that large, well designed randomised controlled trials were needed to confirm them.

But Adrian R Martineau, lead author of the research study, rejected the editorial's conclusion.

“The numbers of people needed to treat with vitamin D to prevent one ARI [acute respiratory infection] are 33 for the estimate from one step individual patient data meta-analysis (IPDMA) and 19 for the estimate from two step IPDMA,” he said. “To put these numbers into context, the NNT [number needed to treat] to prevent one influenza-like illness with parenteral inactivated influenza vaccine is 40 in adults and 28 in children.”

Martineau added, “Influenza vaccination programmes are motivated by the principle that, when a disease is common, even minor reductions in incidence can have significant public health benefits; vitamin D fortification programmes might well be motivated by the same principle, particularly given that ARI is a major cause of industrial absenteeism, health service use, and antibiotic prescribing.

“We acknowledge that the general population may not be motivated to take supplements—this is why we highlight the importance of food fortification as an effective way to boost vitamin D status at a population level.”



1 Martineau AR, Camargo CA, Hooper R. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ* 2017;356:j6583.

Trials Number registry from inception to December 2015.

Eligibility Criteria For study selection

Randomised, double blind, placebo controlled trials of supplementation with vitamin D₃ or vitamin D₂ of any duration were eligible for inclusion if they had been approved by a research ethics committee and if data on incidence of acute respiratory tract infection were collected prospectively and prespecified as an efficacy outcome.

Results

25 eligible randomised controlled trials (total 11 321 participants, aged 0 to 95 years) were identified. IPD were obtained for 10 933 (96.6%) participants. Vitamin D supplementation reduced the risk of acute respiratory tract infection among all participants (adjusted odds ratio 0.88, 95% confidence interval 0.81 to 0.96; P for heterogeneity <0.001). In subgroup analysis, protective effects were seen in those receiving daily or weekly vitamin D without additional bolus doses (adjusted odds ratio 0.81, 0.72 to 0.91) but not in those receiving one or more bolus doses (adjusted odds ratio 0.97, 0.86 to 1.10; P for interaction=0.05). Among those receiving daily or weekly vitamin D, protective effects were stronger in those with baseline 25-hydroxyvitamin D levels <25 nmol/L (adjusted odds ratio 0.30, 0.17 to 0.53) than in those with baseline 25-hydroxyvitamin D levels ≥25 nmol/L (adjusted odds ratio 0.75, 0.60 to 0.95; P for interaction=0.006). Vitamin D did not influence the proportion of participants experiencing at least one serious adverse event (adjusted odds ratio 0.98, 0.80 to 1.20, P=0.83). The body of evidence contributing to these analyses was assessed as being of high quality.

Conclusions

Vitamin D supplementation was safe and it protected against acute respiratory tract infection overall. Patients who were very vitamin D deficient and those not receiving bolus doses experienced the most benefit.

Systematic Review Registration

PROSPERO CRD42014013953.

<https://news.harvard.edu/gazette/story/2017/02/study-confirms-vitamin-d-protects-against-cold-and-flu/>

VITAMIN D and RESPIRATORY TRACT INFECTIONS – Abstracts

[Hormones \(Athens\)](#). 2019 Dec;18(4):353-363. PMID:31768940

The association between vitamin D status and infectious diseases of the respiratory system in infancy and childhood.

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Abstract

PURPOSE: Respiratory tract infections (RTIs) are a major cause of illness worldwide and the most common cause of hospitalization for pneumonia and bronchiolitis. These two diseases are the leading causes of morbidity and mortality among children under 5 years of age. Vitamin D is believed to have immunomodulatory effects on the innate and adaptive immune systems by modulating the expression of antimicrobial peptides, like cathelicidin, in response to both viral and bacterial stimuli. The aim of this review is to summarize the more recently published data with regard to potential associations of 25-hydroxyvitamin D [25(OH)D] with infectious respiratory tract diseases of childhood and the possible health benefits from vitamin D supplementation.

METHODS: The literature search was conducted by using the PubMed, Scopus, and Google Scholar databases, with the following keywords: vitamin D, respiratory tract infection, tuberculosis, influenza, infancy, and childhood.

RESULTS: Several studies have identified links between inadequate 25(OH)D concentrations and the development of upper or lower respiratory tract infections in infants and young children. Some of them also suggest that intervention with vitamin D supplements could decrease both child morbidity and mortality from such causes.

CONCLUSIONS: Most studies agree in that decreased vitamin D concentrations are prevalent among most infants and children with RTIs. Also, normal to high-serum 25(OH)D appears to have some beneficial influence on the incidence and severity of some, but not all, types of these infections. However, studies with vitamin D supplementation revealed conflicting results as to whether supplementation may be of benefit, and at what doses.

[Infect Disord Drug Targets](#). 2019 Jun 26. PMID:31241441

Therapeutic value of Vitamin D as an adjuvant therapy in neonates with sepsis.

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Abstract Sepsis is an unusual systemic reaction to what is sometimes an otherwise ordinary infection, and it probably represents a pattern of response by the immune system to injury. Vitamin D is a fat-soluble steroid hormone that contributes to the maintenance of normal calcium homeostasis and skeletal mineralization. Vitamin D has an important role in the regulation of both innate and adaptive immune systems.

AIM OF THE WORK: Current study aimed to evaluate the therapeutic value of vitamin D supplementation as an adjuvant therapy in neonates with sepsis.

SUBJECTS AND METHOD: This study included 60 neonates with sepsis who were divided into 2 equal groups; group I: 30 neonates with sepsis who received antibiotic only, Group II: 30 neonates with sepsis who received antibiotic therapy and vitamin D. This study included also 30 healthy neonates as a control group. Serum level of 25 (OH) vitamin D and highly sensitive C reactive protein (hs-CRP) were immunoassayed.

RESULTS: There is no significant difference between group I, II and controls as regard weight, gestational age, sex and mode of delivery. There were significant differences between group I and group II in sepsis score and hs-CRP after 3, 7, 10 days of treatment (p values for sepsis score were 0.009, 0.006, 0.004 respectively and for hs-CRP were 0.015, 0.001, 0.001 respectively). There was significance difference in immature /total (I/T) ratio after 7, 10 days of treatment (p value= 0.045, 0.025 respectively) while there was no significance difference in immature /total (I/T) ratio after 3 days of treatment (p value = 0.624). Serum 25(OH) vitamin D levels was significantly lower in neonates with sepsis (group I and II) than controls (p value < 0.05 while there were no significant differences between the three groups as regard serum calcium and phosphorus levels (P =1.000, 1.000 respectively).

Isolated organisms from blood culture in neonates with sepsis (group I and group II) were most commonly B- hemolytic streptococci, E-coli, Hemophilus Influenza and Staphylococcus aureus. There was significant negative correlation between hs-CRP and serum 25 (OH) vitamin D in group II at entry ($r = -0.832$ and P value = 0.001) and after 2 weeks ($r = -0.590$ and P value = 0.021). ROC curve of specificity and sensitivity of 25 (OH) vitamin D level in prediction of early-onset neonatal sepsis shows that cutoff value of vitamin D was ≤ 20 ng/ml, sensitivity 100%, specificity 73%, positive predictive value 73%, negative predictive value 100% and accuracy 87.

CONCLUSION AND RECOMMENDATION: Serum 25 (OH) vitamin D levels of neonates with early onset neonatal sepsis were significantly lower than healthy controls. Vitamin D supplementation improved sepsis score and decrease high levels of hs-CRP; this reflects the role of vitamin D as a target therapy for neonatal sepsis. Further studies are warranted to confirm the therapeutic value of vitamin D in neonatal sepsis.

Influenza Other Respir Viruses. 2019 Mar;13(2):176-183. PMID:30328294 [Free PMC Article](#)

Effect of Vitamin D supplementation to reduce respiratory infections in children and adolescents in Vietnam: A randomized controlled trial.

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Abstract

BACKGROUND: It is uncertain whether vitamin D can reduce respiratory infection.

OBJECTIVE: To determine whether vitamin D supplementation reduces influenza and other upper viral respiratory tract infections.

METHODS: A total of 1300 healthy children and adolescents between the ages of 3 and 17 years were randomized to vitamin D (14 000 U weekly) or placebo for 8 months in Vietnam. The primary outcome was reverse transcriptase (RT)-PCR-confirmed influenza infection, and the coprimary outcome was multiplex PCR-confirmed non-influenza respiratory viruses. Participants, caregivers, and those assessing outcomes were blinded to group assignment.

RESULTS: A total of 650 children and adolescents were randomly assigned to vitamin D and 650 to placebo. The mean baseline serum 25-hydroxyvitamin D levels were 65.7 nmol/L and 65.2 nmol/L in the intervention and placebo groups, respectively, with an increase to 91.8 nmol/L in the vitamin D group and no increase, 64.5 nmol/L, in the placebo group. All 1300 participants randomized contributed to the analysis. We observed RT-PCR-confirmed influenza A or B occurred in 50 children (7.7%) in the vitamin D group and in 43 (6.6%) in the placebo group (hazard ratio [HR]: 1.18, 95% CI: 0.79-1.78). RT-PCR-confirmed non-influenza respiratory virus infection occurred in 146 (22.5%) in the vitamin D group and in 185 (28.5%) in the placebo group (hazard ratio [HR]: 0.76, 95% CI: 0.61-0.94). When considering all respiratory viruses, including influenza, the effect of vitamin D in reducing infection was significant, HR: 0.81, 95% CI: 0.66-0.99.

CONCLUSION: Vitamin D supplementation did not reduce the incidence of influenza but moderately reduced non-influenza respiratory viral infection.

Nutrients. 2019 Mar 7;11(3). pii: E575. PMID:30866564 [Free PMC Article](#)

Vitamin D Deficiency is Associated with Increased Use of Antimicrobials among Preschool Girls in Ethiopia.

[Bodin J](#)^{1,2}, [Mihret A](#)³, [Holm-Hansen C](#)⁴, [Dembinski JL](#)^{5,6}, [Trieu MC](#)^{7,8}, [Tessema B](#)⁹, [Tarekegne A](#)¹⁰, [Yimer SA](#)^{11,12}, [Cox R](#)^{13,14}, [Aseffa A](#)¹⁵, [Haneberg B](#)¹⁶, [Mjaaland S](#)^{17,18}.

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Abstract Preschool children in Addis Ababa, Ethiopia, are highly exposed to influenza viruses. Factors related to infections, nutrition, and environmental conditions that might explain the burden of influenza among these children were investigated. Ninety-five preschool children, 48 girls and 47 boys, were followed clinically for 12 months. Illness and immune responses to influenza; three other respiratory viruses; five airway pathogenic bacteria; and levels of vitamins D, A, and B12 were assessed. Most of the children had antibodies to numerous respiratory viral and bacterial agents at study start, and many were infected during follow-up. Twenty-five girls and 25 boys fell ill during the study, and were treated with one or more courses of systemic antimicrobials. Ninety percent of both girls and boys had 25-hydroxyvitamin D [25(OH)D] levels below the recommended levels. While there was no overall difference in the levels of vitamins D, A, and B12 between girls and boys, treated girls had significantly lower 25(OH)D levels than non-treated girls and treated boys. There was a considerable number of short for age children, but only the short treated girls had significantly lower 25(OH)D levels than the non-treated children. Preschool girls with low 25(OH)D levels were more vulnerable to pathogenic microbes than boys.

Comment: *zinc deficiency associated with short stature and immune deficiency.*

Health Technol Assess. 2019 Jan;23(2):1-44. PMID:30675873 **Free full text**

Vitamin D supplementation to prevent acute respiratory infections: individual participant data meta-analysis.

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Abstract

BACKGROUND: Randomised controlled trials (RCTs) exploring the potential of vitamin D to prevent acute respiratory infections have yielded mixed results. Individual participant data (IPD) meta-analysis has the potential to identify factors that may explain this heterogeneity.

OBJECTIVES: To assess the overall effect of vitamin D supplementation on the risk of acute respiratory infections (ARIs) and to identify factors modifying this effect.

DATA SOURCES: MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, ClinicalTrials.gov and the International Standard Randomised Controlled Trials Number (ISRCTN) registry.

STUDY SELECTION: Randomised, double-blind, placebo-controlled trials of supplementation with vitamin D₃ or vitamin D₂ of any duration having incidence of acute respiratory infection as a pre-specified efficacy outcome were selected.

STUDY APPRAISAL: Study quality was assessed using the Cochrane Collaboration Risk of Bias tool to assess sequence generation, allocation concealment, blinding of participants, personnel and outcome assessors, completeness of outcome data, evidence of selective outcome reporting and other potential threats to validity.

RESULTS: We identified 25 eligible RCTs (a total of 11,321 participants, aged from 0 to 95 years). IPD were obtained for 10,933 out of 11,321 (96.6%) participants. Vitamin D supplementation reduced the risk of ARI among all participants [adjusted odds ratio (aOR) 0.88, 95% confidence interval (CI) 0.81 to 0.96; heterogeneity $p < 0.001$]. Subgroup analysis revealed that protective effects were seen in individuals receiving daily or weekly vitamin D without additional bolus doses (aOR 0.81, 95% CI 0.72 to 0.91), but not in those receiving one or more bolus doses (aOR 0.97, 95% CI 0.86 to 1.10; $p = 0.05$). Among those receiving daily or weekly vitamin D, protective effects of vitamin D were stronger in individuals with a baseline 25-hydroxyvitamin D [25(OH)D] concentration of < 25 nmol/l (aOR 0.30, 95% CI 0.17 to 0.53) than in those with a baseline 25(OH)D concentration of ≥ 25 nmol/l (aOR 0.75, 95% CI 0.60 to 0.95; $p = 0.006$). Vitamin D did not influence the proportion of participants experiencing at least one serious adverse event (aOR 0.98, 95% CI 0.80 to 1.20; $p = 0.83$). The body of evidence contributing to these analyses was assessed as being of high quality.

LIMITATIONS: Our study had limited power to detect the effects of vitamin D supplementation on the risk of upper versus lower respiratory infection, analysed separately.

CONCLUSIONS: Vitamin D supplementation was safe, and it protected against ARIs overall. Very deficient individuals and those not receiving bolus doses experienced the benefit. Incorporation of additional IPD from ongoing trials in the field has the potential to increase statistical power for analyses of secondary outcomes.

J Pediatr. 2017 Aug;187:323-327. PMID:28578159

Low Retinol-Binding Protein and Vitamin D Levels Are Associated with Severe Outcomes in Children Hospitalized with Lower Respiratory Tract Infection and Respiratory Syncytial Virus or Human Metapneumovirus Detection.

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Abstract Retinol binding protein and vitamin D were measured in children aged < 5 years hospitalized with lower respiratory tract infection and respiratory syncytial virus and/or human metapneumovirus detections. Low vitamin levels were observed in 50% of the children and were associated with significantly elevated risk of the need for intensive care unit admission and invasive mechanical ventilation.



Figure 2 Prevalence of vitamin D deficiency/insufficiency in general population worldwide [,,].

[Vitamin D and Infectious Diseases: Simple Bystander or Contributing Factor?](#)

Gois PHE¹ Nutrients. 2017 Jul;9(7):651

Excerpt from Gois 2017:

4. Vitamin D and RTI

Evidence supporting the hypothesis that VDD may predispose to influenza infection derives from observational studies, highlighting the seasonal influence of low sun exposure in both conditions [65,66]. Berry et al. described a linear relationship between VD levels and RTI in a cross-sectional study of 6789 British adults. The authors found that for each 10 nmol/L increase in 25(OH)-VD there was a 7% lower risk of RTI [66]. Accordingly, data from the US Third National Health and Nutrition Examination Survey (NHANES) which included 18,883 adults showed an independent association between serum 25(OH)-VD and recent upper RTI [67]. This correlation was even stronger in individuals with underlying lung disease [67]. Furthermore, similar observations have been reported in other studies, some including children as well as different ethnic groups [68–70].

Clinical trials evaluating the effect of VD supplementation in preventing RTIs have reported contrasting protocols and results. Bergman et al. conducted a systematic review with meta-analysis assessing the effect of VD supplementation on the risk of RTI [33]. Pooled data from 11 RCTs comprising 5660 individuals indicated that VD supplementation is safe and might have a beneficial effect in preventing RTIs [33]. More recently, Martineau et al. published a systematic review with meta-analysis of individual participant data from 25 RCTs including 10,933 subjects [71]. Trials were conducted in 14 countries and 19 out of 25 studies assessed baseline 25(OH)-VD levels. All RCTs supplemented VD₃ orally with different protocols of administration: bolus doses every month to every three months (seven studies using doses ranging from 30,000 to 200,000 IU/month), weekly doses (three studies using doses of 1400, 10,000 and 20,000 IU respectively), daily doses (12 studies using doses ranging from 300 to 4000 IU/day) and a combination of bolus and daily doses (three studies using bolus doses from 96,000 to 120,000 IU and daily doses from 400 to 4000 IU/day). High quality evidence from 25 RCTs with moderate heterogeneity revealed that VD₃ supplementation reduced the risk of experiencing at least one RTI (number needed to treat (NNT) to prevent one episode of RTI = 33, 95% CI 20–101). Furthermore, subgroup analysis of 15 RCTs indicated that daily or weekly VD₃ administration protected against RTI (NNT = 20, 95% CI 13–43), while no protective effect was seen in the 10 RCTs that used bolus doses of VD₃. Moreover, VD₃ supplementation was effective in preventing RTIs irrespective of baseline 25(OH)-VD levels, albeit the protective effects were greatest among subjects with more pronounced VDD [71].

Taken together, the RCT data currently available suggest that VD₃ supplementation may represent a novel and safe indication for preventing RTIs [71]. In addition, daily or weekly doses seem to be more efficient than pulse therapy [33,71]. Finally, individuals with lower levels of VD might benefit more from the supplementation [70,71].

Clin Infect Dis. 2013 Nov;57(10):1384-92. PMID:24014734 [Free PMC Article](#)

Vitamin D3 supplementation and upper respiratory tract infections in a randomized, controlled trial.

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Abstract

BACKGROUND: Randomized controlled trials testing the association between vitamin D status and upper respiratory tract infection (URTI) have given mixed results. During a multicenter, randomized controlled trial of colorectal adenoma chemoprevention, we tested whether **1000 IU/day vitamin D(3) supplementation** reduced winter episodes and duration of URTI and its composite syndromes, influenza-like illness (ILI; fever and ≥ 2 of sore throat, cough, muscle ache, or headache) and colds (no fever, and ≥ 2 of runny nose, nasal congestion, sneezing, sore throat, cough, swollen or tender neck glands).

METHODS: The 2259 trial participants were aged 45–75, in good health, had a history of colorectal adenoma, and had a serum 25-hydroxyvitamin D level ≥ 12 ng/mL. They were randomized to vitamin D(3) (1000 IU/day), calcium (1200 mg/day), both, or placebo. Of these, 759 participants completed daily symptom diaries. Secondary data included semi-annual surveys of all participants.

RESULTS: Among those who completed symptom diaries, supplementation did not significantly reduce winter episodes of URTI (rate ratio [RR], 0.93; 95% confidence interval [CI], .79–1.09) including colds (RR, 0.93; 95% CI, .78–1.10) or ILI (RR, 0.95; 95% CI, .62–1.46), nor did it reduce winter days of

illness (RR, 1.13; 95% CI, .90-1.43). There was no significant benefit according to adherence, influenza vaccination, body mass index, or baseline vitamin D status. Semi-annual surveys of all participants (N = 2228) identified no benefit of supplementation on ILI (odds ratio [OR], 1.14; 95% CI, .84-1.54) or colds (OR, 1.03; 95% CI, .87-1.23).

CONCLUSIONS: Supplementation with 1000 IU/day vitamin D(3) did not significantly reduce the incidence or duration of URTI in adults with a baseline serum 25-hydroxyvitamin D level ≥ 12 ng/mL. *ie.: the dose of Vitamin D3 may have been insufficient to optimise Vit.D levels in the study period (not stated).*

[J Pharmacol Pharmacother. 2012 Oct;3\(4\):300-3. PMID:23326099 Free PMC Article](#)

Vitamin D for prevention of respiratory tract infections: A systematic review and meta-analysis.

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Abstract

OBJECTIVES: To explore the effect of vitamin D supplementation in prevention of respiratory tract infections on the basis of published clinical trials.

MATERIALS AND METHODS: Clinical trials were searched from various electronic databases. Five clinical trials were suitable for inclusion. Outcome was events of respiratory tract infections in vitamin D group and placebo group. Data was reported as odds ratio with 95% confidence interval. Both random and fixed model was used for analysis. Analysis was done with the help of Comprehensive meta-analysis software 2.

RESULTS: Events of respiratory tract infections were significantly lower in vitamin D group as compared to control group [Odds ratio = 0.582 (0.417 - 0.812) P = 0.001] according to random model. Results were similar in fixed model. On separate analysis of clinical trials dealing with groups of children and adults, beneficial effect of vitamin D was observed in both, according to fixed model [Odds ratio = 0.579 (0.416 - 0.805), P = 0.001 and Odds ratio = 0.653 (0.472 - 0.9040, P = 0.010 respectively]. On using random model beneficial effect persisted in children's group but became nonsignificant in adults group [Odds ratio = 0.579 (0.416 - 0.805), P = 0.001 and Odds ratio = 0.544 (0.278 - 1.063) P = 0.075 respectively].

CONCLUSION: Vitamin D supplementation decreases the events related to respiratory tract infections. There is need of more well conducted clinical trials to reach to a certain conclusion.

[Proc Nutr Soc. 2012 Feb;71\(1\):90-7. PMID:22115013](#)

Vitamin D and respiratory infection in adults. [Laaksi J¹](#).

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Abstract Vitamin D insufficiency is a global issue that has significant implications for health. The classical role of vitamin D in bone mineralisation is well known; vitamin D deficiency leads to rickets, osteomalacia or osteoporosis. The role of vitamin D in an immune system is less known. Vitamin D is not an actual vitamin but a secosteroid hormone produced in the skin from 7-dehydrocholesterol after exposure to sunlight UVB radiation. Nutrition and supplements are main sources of vitamin D in wintertime in northern countries as sunlight exposure is inadequate for the production. For activation vitamin D needs to be hydroxylated in liver to form 25-hydroxyvitamin D and in kidney to 1,25-dihydroxyvitamin D, the most active hormone in Ca absorption in the gut. For determination of vitamin D status serum 25-hydroxyvitamin D level, the major circulating form of the hormone is to be measured. Vitamin D regulates gene expression through binding with vitamin D receptors, which dimerises with retinoid X receptor. This complex binds to vitamin D-responsive elements inside the promoter regions of vitamin D-responsive genes. Vitamin D has a key role in innate immunity activation; the production of antimicrobial peptides (cathelicidin and defensins) following Toll-like receptor stimulation by pathogen lipopeptides is dependent on sufficient level of 25-hydroxyvitamin D. Clinically, there is evidence of the association of vitamin D insufficiency and respiratory tract infections. There is also some evidence of the prevention of infections by vitamin D supplementation. Randomised controlled trials are warranted to explore this preventive effect.

[Arch Intern Med. 2009 Feb 23;169\(4\):384-90. PMID:19237723 Free PMC Article](#)

Association between serum 25-hydroxyvitamin D level and upper respiratory tract infection in the Third National Health and Nutrition Examination Survey.

1. [Ginde AA¹](#), [Mansbach JM](#), [Camargo CA Jr](#). *Error! Bookmark not defined.*

Abstract

BACKGROUND: Recent studies suggest a role for vitamin D in innate immunity, including the prevention of respiratory tract infections (RTIs). We hypothesize that serum 25-hydroxyvitamin D (25[OH]D) levels are inversely associated with self-reported recent upper RTI (URTI).

METHODS: We performed a secondary analysis of the Third National Health and Nutrition Examination Survey, a probability survey of the US population conducted between 1988 and 1994. We examined the association between 25(OH)D level and recent URTI in 18 883 participants 12 years and older. The analysis adjusted for demographics and clinical factors (season, body mass index, smoking history, asthma, and chronic obstructive pulmonary disease).

RESULTS: The median serum 25(OH)D level was 29 ng/mL (to convert to nanomoles per liter, multiply by 2.496) (interquartile range, 21-37 ng/mL), and 19% (95% confidence interval [CI], 18%-20%) of participants reported a recent URTI. Recent URTI was reported by 24% of participants with 25(OH)D levels less than 10 ng/mL, by 20% with levels of 10 to less than 30 ng/mL, and by 17% with levels of 30 ng/mL or more ($P < .001$). Even after adjusting for demographic and clinical characteristics, lower 25(OH)D levels were independently associated with recent URTI (compared with 25[OH]D levels of ≥ 30 ng/mL: odds ratio [OR], 1.36; 95% CI, 1.01-1.84 for <10 ng/mL and 1.24; 1.07-1.43 for 10 to <30 ng/mL). The association between 25(OH)D level and URTI seemed to be stronger in individuals with asthma and chronic obstructive pulmonary disease (OR, 5.67 and 2.26, respectively).

CONCLUSIONS: Serum 25(OH)D levels are inversely associated with recent URTI. This association may be stronger in those with respiratory tract diseases. Randomized controlled trials are warranted to explore the effects of vitamin D supplementation on RTI.

VITAMIN D and INFLUENZA - Abstracts

Inflamm Bowel Dis. 2019 May 4;25(6):1088-1095. PMID:30601999 [Free PMC Article](#)

Randomized Trial of Vitamin D Supplementation to Prevent Seasonal Influenza and Upper Respiratory Infection in Patients with Inflammatory Bowel Disease.

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Abstract

BACKGROUND: We evaluated whether oral vitamin D supplementation during the winter and early spring reduces the incidence of influenza and upper respiratory infections in patients with inflammatory bowel disease (IBD).

METHODS: A randomized, double-blind, controlled trial was conducted to compare the effects of vitamin D supplementation (500 IU/day) and a placebo. The primary outcome was the incidence of influenza; the secondary outcome was the incidence of upper respiratory infection. Prespecified subgroup analyses were performed according to 25-hydroxyvitamin D (25-OHD) levels (low <20 ng/mL or high ≥20 ng/mL) and whether ulcerative colitis (UC) or Crohn's disease (CD) was present. We also used the Lichtiger clinical activity index for patients with UC and the Crohn's Disease Activity Index (CDAI) for patients with CD before and after interventions.

RESULTS: We included 223 patients with IBD and randomized them into 2 groups: vitamin D supplementation (n = 108) and placebo (n = 115). The incidence of influenza did not differ between the groups. However, the incidence of upper respiratory infection was significantly lower in the vitamin D group (relative risk [RR], 0.59; 95% confidence interval (CI), 0.35-0.98; P = 0.042). This effect was enhanced in the low 25-OHD level subgroup (RR, 0.36; 95% CI, 0.14-0.90; P = 0.02). With respect to adverse events, the Lichtiger clinical activity index score was significantly worse in the vitamin D group (P = 0.002) and remained significant only in the high 25-OHD level subgroup.

CONCLUSIONS: Vitamin D supplementation may have a preventative effect against upper respiratory infection in patients with IBD but may worsen the symptoms of UC.

Influenza Other Respir Viruses. 2019 Mar;13(2):176-183. PMID:30328294 [Free PMC Article](#)

Effect of Vitamin D supplementation to reduce respiratory infections in children and adolescents in Vietnam: A randomized controlled trial.

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Abstract

BACKGROUND: It is uncertain whether vitamin D can reduce respiratory infection.

OBJECTIVE: To determine whether vitamin D supplementation reduces influenza and other upper viral respiratory tract infections.

METHODS: A total of 1300 healthy children and adolescents between the ages of 3 and 17 years were randomized to vitamin D (14 000 U weekly) or placebo for 8 months in Vietnam. The primary outcome was reverse transcriptase (RT)-PCR-confirmed influenza infection, and the coprimary outcome was multiplex PCR-confirmed non-influenza respiratory viruses. Participants, caregivers, and those assessing outcomes were blinded to group assignment.

RESULTS: A total of 650 children and adolescents were randomly assigned to vitamin D and 650 to placebo. The mean baseline serum 25-hydroxyvitamin D levels were 65.7 nmol/L and 65.2 nmol/L in

the intervention and placebo groups, respectively, with an increase to 91.8 nmol/L in the vitamin D group and no increase, 64.5 nmol/L, in the placebo group. All 1300 participants randomized contributed to the analysis. We observed RT-PCR-confirmed influenza A or B occurred in 50 children (7.7%) in the vitamin D group and in 43 (6.6%) in the placebo group (hazard ratio [HR]: 1.18, 95% CI: 0.79-1.78). RT-PCR-confirmed non-influenza respiratory virus infection occurred in 146 (22.5%) in the vitamin D group and in 185 (28.5%) in the placebo group (hazard ratio [HR]: 0.76, 95% CI: 0.61-0.94). When considering all respiratory viruses, including influenza, the effect of vitamin D in reducing infection was significant, HR: 0.81, 95% CI: 0.66-0.99.

CONCLUSION: Vitamin D supplementation did not reduce the incidence of influenza but moderately reduced non-influenza respiratory viral infection.

Nutrients. 2019 Mar 7;11(3). pii: E575. PMID:30866564 [Free PMC Article](#)

Vitamin D Deficiency is Associated with Increased Use of Antimicrobials among Preschool Girls in Ethiopia.

[Bodin J](#)^{1,2}, [Mihret A](#)³, [Holm-Hansen C](#)⁴, [Dembinski JL](#)^{5,6}, [Trieu MC](#)^{7,8}, [Tessema B](#)⁹, [Tarekegne A](#)¹⁰, [Yimer SA](#)^{11,12}, [Cox R](#)^{13,14}, [Aseffa A](#)¹⁵, [Haneberg B](#)¹⁶, [Mjaaland S](#)^{17,18}.

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Abstract Preschool children in Addis Ababa, Ethiopia, are highly exposed to influenza viruses.

Factors related to infections, nutrition, and environmental conditions that might explain the burden of influenza among these children were investigated. Ninety-five preschool children, 48 girls and 47 boys, were followed clinically for 12 months. Illness and immune responses to influenza; three other respiratory viruses; five airway pathogenic bacteria; and levels of vitamins D, A, and B12 were assessed. Most of the children had antibodies to numerous respiratory viral and bacterial agents at study start, and many were infected during follow-up. Twenty-five girls and 25 boys fell ill during the study, and were treated with one or more courses of systemic antimicrobials. Ninety percent of both girls and boys had 25-hydroxyvitamin D [25(OH)D] levels below the recommended levels. While there was no overall difference in the levels of vitamins D, A, and B12 between girls and boys, treated girls had significantly lower 25(OH)D levels than non-treated girls and treated boys. There was a considerable number of short for age children, but only the short treated girls had significantly lower 25(OH)D levels than the non-treated children. Preschool girls with low 25(OH)D levels were more vulnerable to pathogenic microbes than boys.

Comment: zinc deficiency associated with short stature and immune deficiency.

Pediatr Infect Dis J. 2018 Jan 8. PMID:29315160

Preventive Effects of Vitamin D on Seasonal Influenza A in Infants: A Multicenter, Randomized, Open, Controlled Clinical Trial.

[Zhou J](#)¹, [Du J](#)¹, [Huang L](#)², [Wang Y](#)³, [Shi Y](#)³, [Lin H](#)².

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2 Department Of Pediatrics, The Second Affiliated Hospital And Yuying Children's Hospital Of Wenzhou Medical University, Wenzhou, China.

3 Department Of Pediatrics, Jinhua People's Hospital, Jinhua, China.

Abstract

OBJECTIVES: This study aimed to evaluate the clinical efficacy and safety of vitamin D for preventing influenza A in 400 infants in a multicenter, randomized, open, controlled clinical trial.

METHODS: The infants were randomized into low-dose and high-dose vitamin D groups, and serum calcium, inorganic phosphorus and 25-hydroxyvitamin D levels were detected thrice in 4 months.

Infants infected with influenza A were monitored for symptoms including fever, cough, and wheezing. Pathogen levels and safety of vitamin D treatment were also evaluated.

RESULTS: Of 121 cases in total, 78 and 43 cases of influenza A infection occurred in the low-dose and high-dose vitamin D groups, respectively. There was a significant difference between the groups ($\chi^2 = 14.6324$, $P = 0.0001$). Among the cases of influenza infection, the median durations for fever, cough, and wheezing were shorter in the high-dose vitamin D group than in the low-dose vitamin D group. The viral loads showed a downward trend in both groups, and were significantly different between the groups at the second and third detections. Additionally, the incidences of adverse events and severe adverse events were very low and not significantly different between the two groups.

CONCLUSION: High-dose vitamin D (1200 IU) is suitable for the prevention of seasonal influenza as evidenced by rapid relief from symptoms, rapid decrease in viral loads, and disease recovery. In addition, high-dose vitamin D is probably safe for infants.

[Int J Mol Sci. 2018 Aug 16;19\(8\). pii: E2419. PMID:30115864](#)

Vitamin D and Influenza-Prevention or Therapy? [Gruber-Bzura BM¹](#).

1 Department of Biochemistry and Biopharmaceuticals, National Medicines Institute, Str. Chelmska 30/34, 00-725 Warsaw, Poland. b.gruber@nil.gov.pl.

Abstract Vitamin D generates many extra-skeletal effects due to the vitamin D receptor (VDR) which is present in most tissues throughout the body. The possible role of vitamin D in infections is implied from its impact on the innate and adaptive immune responses. A significant effect is also the suppression of inflammatory processes. Because vitamin D could be acknowledged as a "seasonal stimulus", as defined by R. Edgar Hope-Simpson, it would be crucial to prove it from a potential easy and cheap prophylaxis or therapy support perspective as far as influenza infections are concerned. The survey of the literature data generates some controversies and doubts about the possible role of vitamin D in the prevention of influenza virus. The most important point is to realise that the broad spectrum of this vitamin's activity does not exclude such a possibility. According to most of the authors, more randomized controlled trials with effective, large populations are needed to explore the preventive effect of vitamin D supplementation on viral influenza infections.

[Clin Nutr. 2017 Oct;36\(5\):1288-1293. PMID:27595379](#)

Association of serum 25-hydroxyvitamin D with influenza in case-control study nested in a cohort of Japanese employees.

[Nanri A¹](#), [Nakamoto K²](#), [Sakamoto N³](#), [Imai T⁴](#), [Akter S⁵](#), [Nonaka D⁶](#), [Mizoue T⁵](#).

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6 Department of Global Health, School of Health Sciences, University of the Ryukyus, Okinawa, Japan.

Abstract

BACKGROUND & AIMS: Several intervention studies have examined the effect of vitamin D supplementation on influenza or influenza-like illness, but their results have been inconsistent. We prospectively examined the association of serum 25-hydroxyvitamin D with influenza among Japanese workers.

METHODS: We conducted a nested case-control study in a cohort of workers in 4 companies in the Kanto and Tokai areas of Japan. Physician-diagnosed influenza that occurred during the winter season was ascertained using a self-administered questionnaire. Two controls matched by company, sex, and age (and checkup date in 1 company) were selected for each case. Serum 25-hydroxyvitamin D concentrations at baseline were measured using a competitive protein binding assay. Odds ratio of influenza were estimated by conditional logistic regression with adjustment for covariates.

RESULTS: Of 182 cases and 364 controls, 179 cases and 353 controls with complete data were included in the analysis. Serum 25-hydroxyvitamin D concentrations were not associated with a significantly lower risk of influenza; the multivariable-adjusted odds ratio for the highest (≥ 30 ng/mL) versus lowest category (< 20 ng/mL) was 0.77 (95% confidence interval 0.37-1.59) (P for trend = 0.80).

In a subgroup of participants without vaccination, vitamin D sufficiency (≥ 30 ng/mL) was associated with a significantly lower risk of influenza (odds ratio 0.14; 95% confidence interval 0.03-0.74).

CONCLUSIONS: Overall, circulating 25-hydroxyvitamin D concentrations were not appreciably associated with influenza episodes. However, the lower influenza risk associated with vitamin D sufficiency among unvaccinated participants warrants further investigation.

Key observation: Optimal Vitamin D levels are associated with lower risk of influenza in unvaccinated, but not in vaccinated individuals.

J Nepal Health Res Counc. 2016 Jan;14(32):69-70. PMID:27426715

Indoor Staying During Winter Season Makes People More Susceptible to Flu.

Acharya B¹, Thapa K².

¹ Central Department of Microbiology, Tribhuvan University, Kirtipur, Nepal.

² HOPE International College, Lalitpur, Nepal.

Abstract An infectious diseases caused by RNA virus, the influenza is also commonly known as Flu. It mainly transmitted through air by coughs or sneezes of infected. The symptoms of flu like fever and headache are the result of the huge amounts of proinflammatory cytokines and chemokines (such as interferon or tumor necrosis factor) produced from influenza-infected cells. The activated vitamin has extreme effects on human immunity. Vitamin D prevents too much release of cytokines and chemokines. Staying much time indoor, away from contact of sunlight during winter season lowers the vitamin D level in human body. Thus, the chance of getting flu increases in winter season. Formulation of policy regarding vitamin D supplementation in diet for people such as elderly and with low sunlight exposure is hereby recommended. It will be beneficial to reduce influenza related morbidity and mortality during winter season.

Vitamin D for influenza

Can Fam Physician. 2015 Jun; 61(6): 507. Gerry Schwalfenberg,..

Excerpt

"A colleague of mine and I have introduced vitamin D at doses that have achieved greater than 100 nmol/L in most of our patients for the past number of years, and we now see very few patients in our clinics with the flu or influenza-like illness. In those patients who do have influenza, we have treated them with the *vitamin D hammer*, as coined by my colleague. This is a 1-time 50 000 IU dose of vitamin D3 or 10 000 IU 3 times daily for 2 to 3 days. The results are dramatic, with complete resolution of symptoms in 48 to 72 hours. One-time doses of vitamin D at this level have been used safely and have never been shown to be toxic.⁸ We urgently need a study of this intervention. The cost of vitamin D is about a penny for 1000 IU, so this treatment costs less than a dollar".

Food Funct. 2014 Sep;5(9):2365-70. PMID:25088394

Effects of vitamin D supplements on influenza A illness during the 2009 H1N1 pandemic: a randomized controlled trial.

Urashima M¹, Mezawa H, Noya M, Camargo CA Jr.

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Abstract. In a prior randomized trial, we found that the incidence of influenza A was less in the vitamin D3 group than among those on placebo, but the total incidence of either influenza A or B did not differ between groups. In this trial, the incidence of influenza A or B was less in the vitamin D3 group than in the placebo group only during the first half of the study. To elucidate whether vitamin D3 has preventive actions against influenza A, we conducted another trial during the 2009 pandemic of the H1N1 subtype of influenza A. Students (n = 247) of a Japanese high school were randomly assigned to receive vitamin D3 supplements (n = 148; **2000 IU per day**) or a placebo (n = 99) in a double-blind study for 2 months. The primary outcome was incidence of influenza A diagnosed by a rapid influenza diagnostic test by medical doctors. Influenza A was equally likely in the vitamin D3 group (20/148: 13.5%) compared with the placebo group (12/99: 12.1%). **By post hoc analysis, influenza A occurred significantly less in the vitamin D3 group (2/148: 1.4%) compared with the placebo group (8/99: 8.1%) (risk ratio, 0.17; 95% confidence interval, 0.04 to 0.77; P = 0.009) in the first month.** However, during the second month, the vitamin D3 group experienced more events and effectively caught up with the placebo group. Vitamin D3 supplementation lowered the overall incidence of influenza A during the

2009 H1N1 pandemic. A post hoc analysis suggests that the initial benefit during the first month of treatment was lost during the second month.

Adv Nutr. 2012 Jul 1;3(4):517-25. PMID:22797987 [Free PMC Article](#)

Vitamin D and influenza. [Sundaram ME¹](#), [Coleman LA](#).

¹ Marshfield Clinic Research Foundation, Marshfield, WI, USA. sundaram.maria@marshfieldclinic.org

Abstract. Vitamin D has become increasingly recognized in the literature for its extra-skeletal roles, including an effect on inflammation and the immune response to infection. Our goal was to describe the role of vitamin D in the immune response and implications for the risk of influenza infection in humans. In this review, we first consider literature that provides molecular and genetic support to the idea that vitamin D is related to the adaptive and innate immune responses to influenza infection in vitro and in animal models. We then discuss observational studies and randomized controlled trials of vitamin D supplementation in humans. Finally, we consider some of the knowledge gaps surrounding vitamin D and immune response that must be filled.

Scand J Infect Dis. 2012 Feb;44(2):126-32. PMID:22026455 [Free PMC Article](#)

Vitamin D supplementation did not prevent influenza-like illness as diagnosed retrospectively by questionnaires in subjects participating in randomized clinical trials.

[Jorde R¹](#), [Witham M](#), [Janssens W](#), [Rolighed L](#), [Borchhardt K](#), [de Boer IH](#), [Grimnes G](#), [Hutchinson MS](#).

¹ Endocrinology Research Group, Institute of Clinical Medicine, University of Tromsø, and Medical Clinic, University Hospital of North Norway, Tromsø, Norway. rolf.jorde@unn.no

Abstract

BACKGROUND: Vitamin D deficiency has been associated with a number of diseases, including influenza. Whether or not this reflects a causal relationship is unknown. We therefore wanted to examine if supplementation with vitamin D would affect the incidence and severity of influenza-like disease.

METHODS: Questionnaires on influenza were sent to subjects participating in ongoing placebo-controlled intervention studies with vitamin D supplementation, up until the end of April 2010.

RESULTS: Five hundred and sixty-nine subjects from 10 different clinical trials were included in the study, of whom 289 were randomized to receive vitamin D (1111-6800 IU/day) and 280 to receive placebo. Influenza-like disease during the previous fall/winter was reported in 38 subjects in the vitamin D group and 42 in the placebo group (non-significant), of whom 25 and 26 subjects, respectively, fulfilled our clinical criteria for influenza. In these latter subjects, the duration of illness was significantly longer among those in the vitamin D group than among those in the placebo group (median 7 (range 2-60) days vs median 4 (range 2-18) days; $p = 0.007$). However, this difference was not statistically significant if all 38 (vitamin D) and 42 (placebo) subjects who reported symptoms were included.

CONCLUSION: Our results do not support the hypothesis that high doses of vitamin D supplementation will have a pronounced effect on influenza-like disease in populations not targeted for high influenza risk.

Table II

Details of intervention studies included.

Location	Subjects	Main outcome measure	Intervention
Tromsø 1, Norway	Subjects with reduced glucose tolerance	Development of type 2 diabetes	20,000 IU vitamin D3 per week or placebo
Tromsø 2, Norway	Subjects with serum 25(OH)D < 50 nmol/l	Blood pressure, lipids, depression	40,000 IU vitamin D3 per week or placebo
Tromsø 3, Norway	Subjects with serum 25(OH)D < 50 nmol/l	Glucose sensitivity	40,000 IU vitamin D3 per week or placebo

Location	Subjects	Main outcome measure	Intervention
Vienna, Austria	Kidney transplant recipients with 25(OH)D < 50 nmol/l	Graft function	6800 IU vitamin D3 per day or placebo
Seattle, USA	Type 2 diabetes with 25(OH) D < 75 nmol/l and urine albumin excretion ≥ 30 mg/day	Urine albumin excretion	2000 IU vitamin D3 per day or placebo
Dundee 1, Scotland	Age > 70 y, isolated systolic hypertension and 25(OH)D < 75 nmol/l	Blood pressure	100,000 units vitamin D3 or placebo, taken at 0, 3, 6, and 9 months
Dundee 2, Scotland	Adults with a past history of myocardial infarction	Change in endothelial function	100,000 units vitamin D3 or placebo, taken at 0, 2, and 4 months
Dundee 3, Scotland	Adults with resistant hypertension and 25(OH)D level < 75 nmol/l	Blood pressure	100,000 units vitamin D3 or placebo, taken at 0, 2, and 4 months
Aarhus, Denmark	Subjects with serum 25(OH) D < 80 nmol/l	PTH and calcium metabolism	2800 IU vitamin D3 per day or placebo
Leuven, Belgium	Patients with moderate to very severe COPD	COPD exacerbations	100,000 units vitamin D3 or placebo every 4 weeks during 1 y

25(OH)D, 25-hydroxyvitamin D; PTH, parathyroid hormone; COPD, chronic obstructive pulmonary disease.

Comment – *no differentiation between vaccinated and unvaccinated subjects in response to Vitamin D;*
 - *Dose-response of variable doses of Vitamin D3 not assessed;*
 - *No estimation of Vit D serum levels.*

Am J Clin Nutr. 2010 May;91(5):1255-60. PMID:20219962

Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren.

[Urashima M](#)¹, [Segawa T](#), [Okazaki M](#), [Kurihara M](#), [Wada Y](#), [Ida H](#).

¹ Division of Molecular Epidemiology, Jikei University School of Medicine, Nishi-shimbashi 3-25-8, Minato-ku, Tokyo 105-8461, Japan. urashima@jikei.ac.jp

Abstract

BACKGROUND: To our knowledge, no rigorously designed clinical trials have evaluated the relation between vitamin D and physician-diagnosed seasonal influenza.

OBJECTIVE: We investigated the effect of vitamin D supplements on the incidence of seasonal influenza A in schoolchildren.

DESIGN: From December 2008 through March 2009, we conducted a randomized, double-blind, placebo-controlled trial comparing vitamin D(3) supplements (1200 IU/d) with placebo in schoolchildren. The primary outcome was the incidence of influenza A, diagnosed with influenza antigen testing with a nasopharyngeal swab specimen.

RESULTS: Influenza A occurred in 18 of 167 (10.8%) children in the vitamin D(3) group compared with 31 of 167 (18.6%) children in the placebo group [relative risk (RR), 0.58; 95% CI: 0.34, 0.99; P = 0.04]. The reduction in influenza A was more prominent in children who had not been taking other vitamin D supplements (RR: 0.36; 95% CI: 0.17, 0.79; P = 0.006) and who started nursery school after age 3 y (RR: 0.36; 95% CI: 0.17, 0.78; P = 0.005). In children with a previous diagnosis of asthma, asthma attacks as a secondary outcome occurred in 2 children receiving vitamin D(3) compared with 12 children receiving placebo (RR: 0.17; 95% CI: 0.04, 0.73; P = 0.006).

CONCLUSION: This study suggests that vitamin D(3) supplementation during the winter may reduce the incidence of influenza A, especially in specific subgroups of schoolchildren. This trial was registered at <https://center.umin.ac.jp> as UMIN000001373.

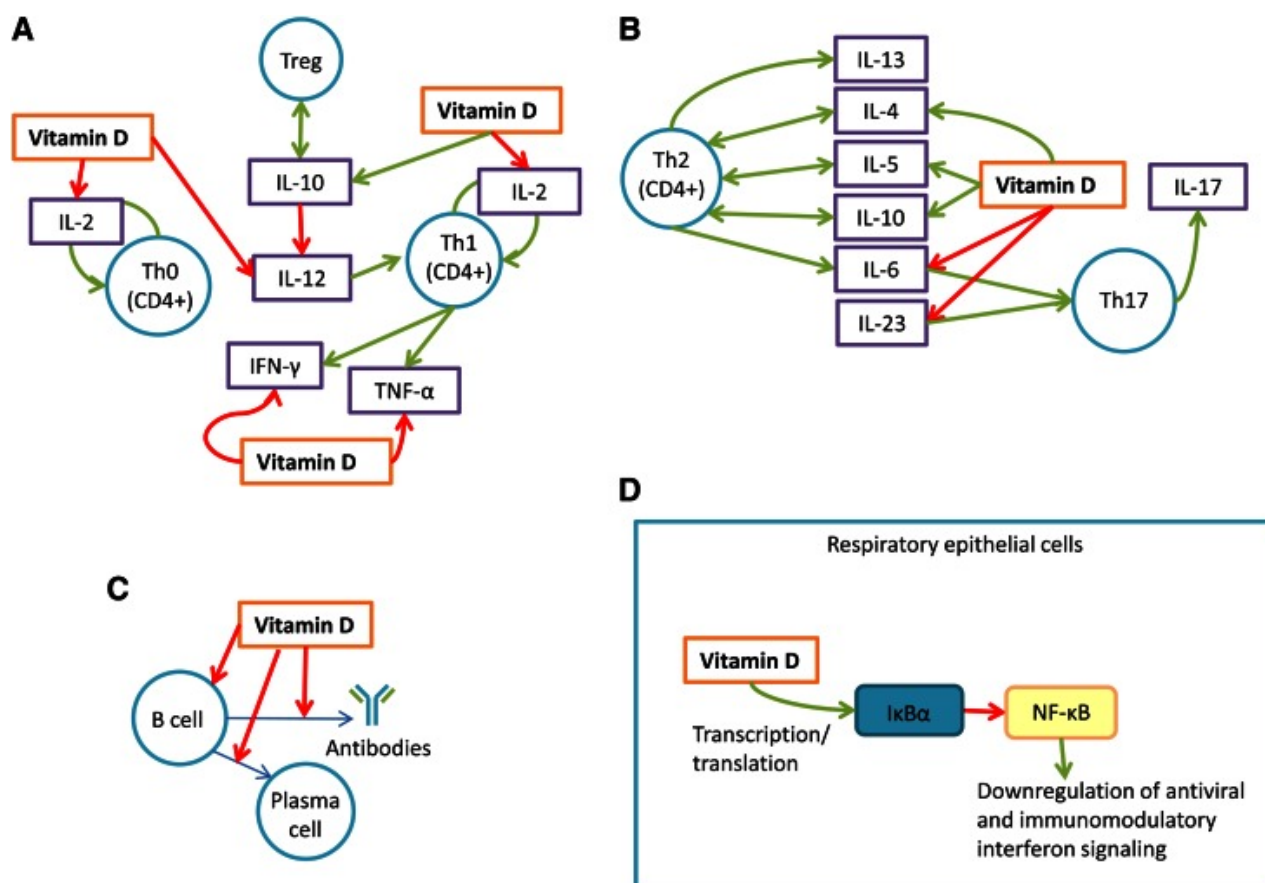


Figure 1 Vitamin D and its various actions in the immune system. (A) Vitamin D inhibits the production and proliferation of Th1 and Th0 cells by inhibiting IL-2, IFN-γ, and TNF-α; vitamin D promotes the production of Treg cells by facilitating production of IL-10. (B) Vitamin D promotes a Th2-mediated immune response profile by promoting IL-4, IL-5, and IL-10. Vitamin D inhibits a Th17-mediated immune response profile (and thus inhibits IL-17) by inhibiting IL-6 and IL-23. (C) Vitamin D inhibits the production of B cells, the differentiation of B cells into plasma cells, and the production of antibodies by B cells. (D) Vitamin D promotes nuclear factor of kappa light polypeptide gene enhancer in B cells inhibitor, α in respiratory epithelial cells, which inhibits NF-κB, in turn promoting antiviral and immunomodulatory interferon signaling. Th, T helper cell; Treg, T regulatory cell.

[Vitamin D and Influenza](#) Adv Nutr. 2012 Jul;3(4):517-525.

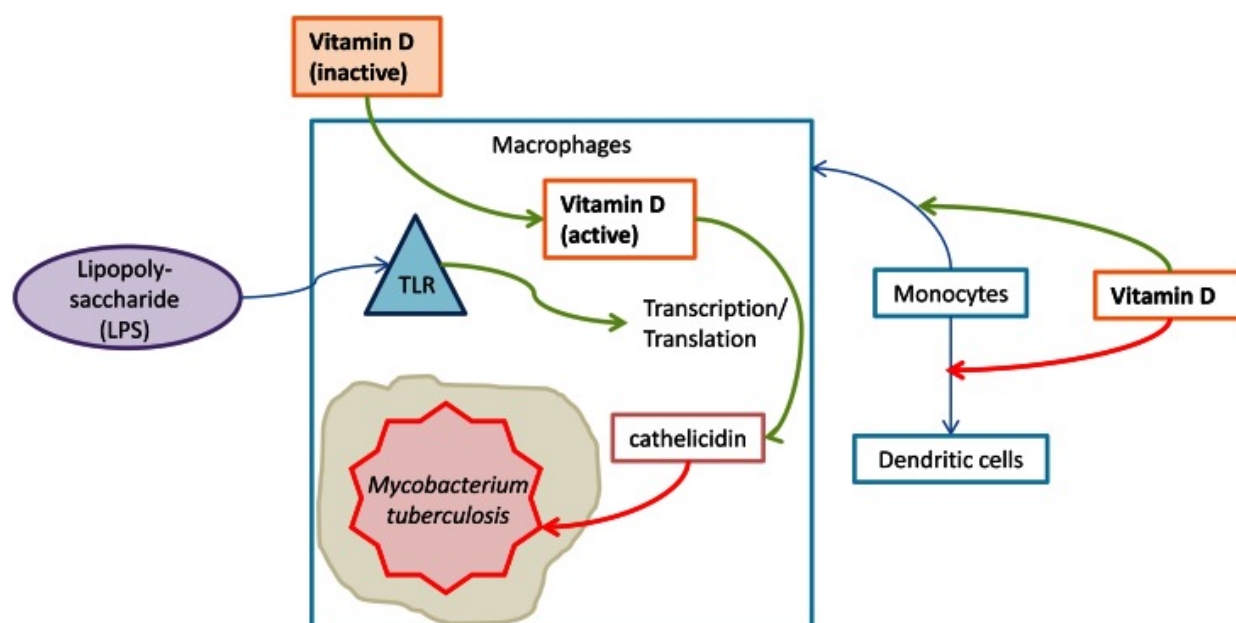


Figure 2 Vitamin D activation and mycobacterial immune response. Vitamin D inhibits the differentiation of monocytes into dendritic cells and promotes the differentiation of monocytes into macrophages. When toll-like receptors are activated by circulating LPS, they promote vitamin D-

mediated transcription of cathelicidin, an antimicrobial peptide that kills *Mycobacterium tuberculosis*.
[Vitamin D and Influenza](#) Adv Nutr. 2012 Jul;3(4):517-525.

[Int J Infect Dis.](#) 2010 Dec;14(12):e1099-105. PMID:21036090 **Free full text**

The seasonality of pandemic and non-pandemic influenzas: the roles of solar radiation and vitamin D.

[Juzeniene A¹](#), [Ma LW](#), [Kwitniewski M](#), [Polev GA](#), [Lagunova Z](#), [Dahlback A](#), [Moan J](#).

¹ Department of Radiation Biology, Institute for Cancer Research, the Norwegian Radium Hospital, Oslo University Hospital, Montebello, N-0310 Oslo, Norway. asta.juzeniene@rr-research.no

Abstract

OBJECTIVES: Seasonal variations in ultraviolet B (UVB) radiation cause seasonal variations in vitamin D status. This may influence immune responses and play a role in the seasonality of influenza.

METHODS: Pandemic and non-pandemic influenzas in Sweden, Norway, the USA, Singapore, and Japan were studied. Weekly/monthly influenza incidence and death rates were evaluated in view of monthly UVB fluences.

RESULTS: Non-pandemic influenzas mostly occur in the winter season in temperate regions. UVB calculations show that at high latitudes very little, if any, vitamin D is produced in the skin during the winter. Even at 26°N (Okinawa) there is about four times more UVB during the summer than during the winter. In tropical regions there are two minor peaks in vitamin D photosynthesis, and practically no seasonality of influenza. Pandemics may start with a wave in an arbitrary season, while secondary waves often occur the following winter. Thus, it appears that a low vitamin D status may play a significant role in most influenzas.

CONCLUSIONS: In temperate latitudes even pandemic influenzas often show a clear seasonality. The data support the hypothesis that high influences of UVB radiation (vitamin D level), as occur in the summer, act in a protective manner with respect to influenza.

[Mol Nutr Food Res.](#) 2010 Aug;54(8):1072-6. PMID:20440692

Vitamin D supplementation in a nursing home population.

[Schwalfenberg GK¹](#), [Genuis SJ](#).

¹ Department of Family Practice, University of Alberta, Edmonton, Alberta, Canada. gschwalf@telus.net

Abstract To determine if daily supplementation of 2000 IU of vitamin D(3) is able to normalize the 25(OH)D(3) status in a nursing home population, a group particularly prone to Vitamin D insufficiency. A chart review was performed to retrospectively determine the 25(OH)D(3) level in each nursing home patient (N=68) who had received a minimum of 5 months of daily 2000 IU vitamin D(3) supplementation. 94.1% of nursing home residents had a 25(OH)D(3) level in excess of 80 nmol/L after a minimum of 5 months of daily 2,000 IU vitamin D(3) supplementation. No residents had 25(OH)D(3) levels in a toxic range. In order to improve health and well-being and to preclude preventable morbidity and mortality associated with 25(OH)D(3) insufficiency, all nursing home patients without contraindication should be routinely supplemented with (at minimum) 2000 IU of vitamin D(3) on a daily basis.

[Am J Clin Nutr.](#) 2010 May;91(5):1255-60. PMID:20219962 **Free full text**

Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren.

[Urashima M¹](#), [Segawa T](#), [Okazaki M](#), [Kurihara M](#), [Wada Y](#), [Ida H](#).

¹ Division of Molecular Epidemiology, Jikei University School of Medicine, Nishi-shimbashi 3-25-8, Minato-ku, Tokyo 105-8461, Japan. urashima@jikei.ac.jp

Abstract

BACKGROUND: To our knowledge, no rigorously designed clinical trials have evaluated the relation between vitamin D and physician-diagnosed seasonal influenza.

OBJECTIVE: We investigated the effect of vitamin D supplements on the incidence of seasonal influenza A in schoolchildren.

DESIGN: From December 2008 through March 2009, we conducted a randomized, double-blind, placebo-controlled trial comparing vitamin D(3) supplements (1200 IU/d) with placebo in schoolchildren. The primary outcome was the incidence of influenza A, diagnosed with influenza antigen testing with a nasopharyngeal swab specimen.

RESULTS: Influenza A occurred in 18 of 167 (10.8%) children in the vitamin D(3) group compared with 31 of 167 (18.6%) children in the placebo group [relative risk (RR), 0.58; 95% CI: 0.34, 0.99; P = 0.04].

The reduction in influenza A was more prominent in children who had not been taking other vitamin D supplements (RR: 0.36; 95% CI: 0.17, 0.79; P = 0.006) and who started nursery school after age 3 y (RR: 0.36; 95% CI: 0.17, 0.78; P = 0.005). In children with a previous diagnosis of asthma, asthma attacks as a secondary outcome occurred in 2 children receiving vitamin D(3) compared with 12 children receiving placebo (RR: 0.17; 95% CI: 0.04, 0.73; P = 0.006).

CONCLUSION: This study suggests that vitamin D(3) supplementation during the winter may reduce the incidence of influenza A, especially in specific subgroups of schoolchildren.

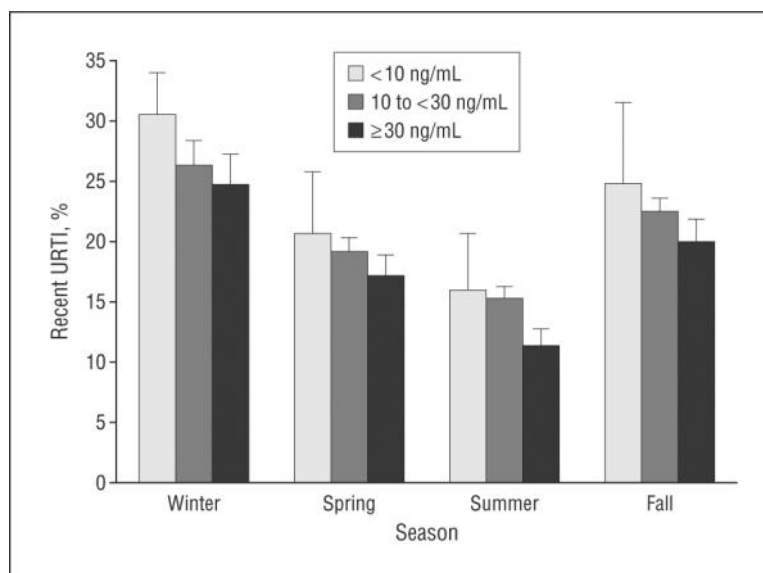


Figure 1 Participants with recent upper respiratory tract infection (URTI) stratified by serum 25-hydroxyvitamin D level (to convert to nanomoles per liter, multiply by 2.496) and season. Error bars represent standard errors of estimates. [Association Between Serum 25-Hydroxyvitamin D Level and Upper Respiratory Tract Infection in the Third National Health and Nutrition Examination Survey](#) Arch Intern Med. ;169(4):384-390.

Epidemiol Infect. 2006 Dec;134(6):1129-40. PMID:16959053 [Free PMC Article](#)

Epidemic influenza and vitamin D.

[Cannell JJ¹](#), [Vieth R](#), [Umhau JC](#), [Holick MF](#), [Grant WB](#), [Madronich S](#), [Garland CF](#), [Giovannucci E](#).

¹ Atascadero State Hospital, 10333 El Camino Real, Atascadero, CA 93422, USA. jcannell@dmhash.state.ca.us

Abstract In 1981, R. Edgar Hope-Simpson proposed that a 'seasonal stimulus' intimately associated with solar radiation explained the remarkable seasonality of epidemic influenza. Solar radiation triggers robust seasonal vitamin D production in the skin; vitamin D deficiency is common in the winter, and activated vitamin D, 1,25(OH)₂D, a steroid hormone, has profound effects on human immunity. 1,25(OH)₂D acts as an immune system modulator, preventing excessive expression of inflammatory cytokines and increasing the 'oxidative burst' potential of macrophages. Perhaps most importantly, it dramatically stimulates the expression of potent anti-microbial peptides, which exist in neutrophils, monocytes, natural killer cells, and in epithelial cells lining the respiratory tract where they play a major role in protecting the lung from infection. Volunteers inoculated with live attenuated influenza virus are more likely to develop fever and serological evidence of an immune response in the winter. Vitamin D deficiency predisposes children to respiratory infections. Ultraviolet radiation (either from artificial sources or from sunlight) reduces the incidence of viral respiratory infections, as does cod liver oil (which contains vitamin D). An interventional study showed that vitamin D reduces the incidence of respiratory infections in children. We conclude that vitamin D, or lack of it, may be Hope-Simpson's 'seasonal stimulus'.

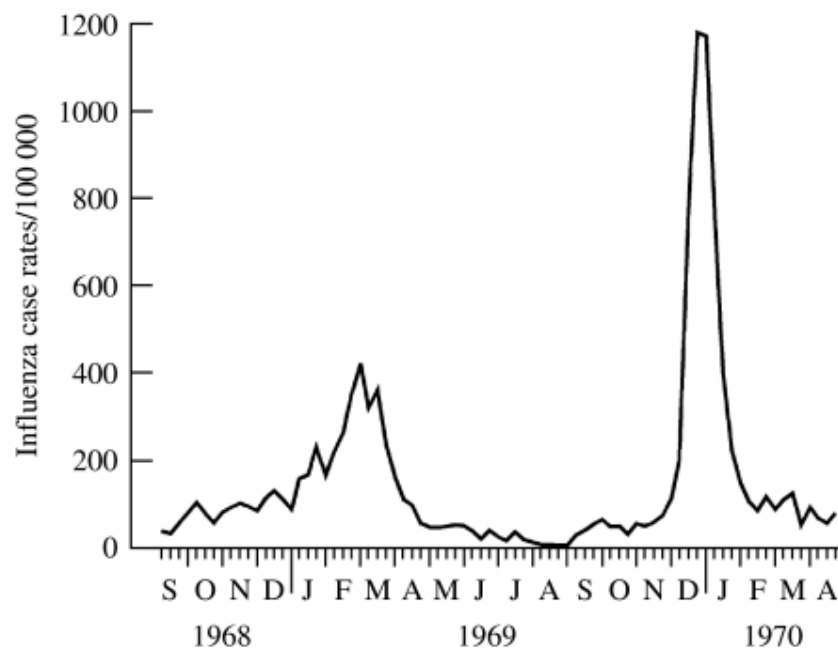


Fig.2 Weekly consultation rates for illnesses diagnosed clinically as influenza or influenza-like, calculated from returns to the General Practice Research Unit of the Royal College of General Practitioners from about 40 general practices in various parts of England, Scotland and Wales, serving a population of about 150 000 persons, 1968–1970. (Reproduced/amended with permission, BMJ Publishing Group, Miller *et al.*)

[Epidemic influenza and vitamin D](#) Epidemiol Infect. 2006 Dec;134(6):1129-1140.

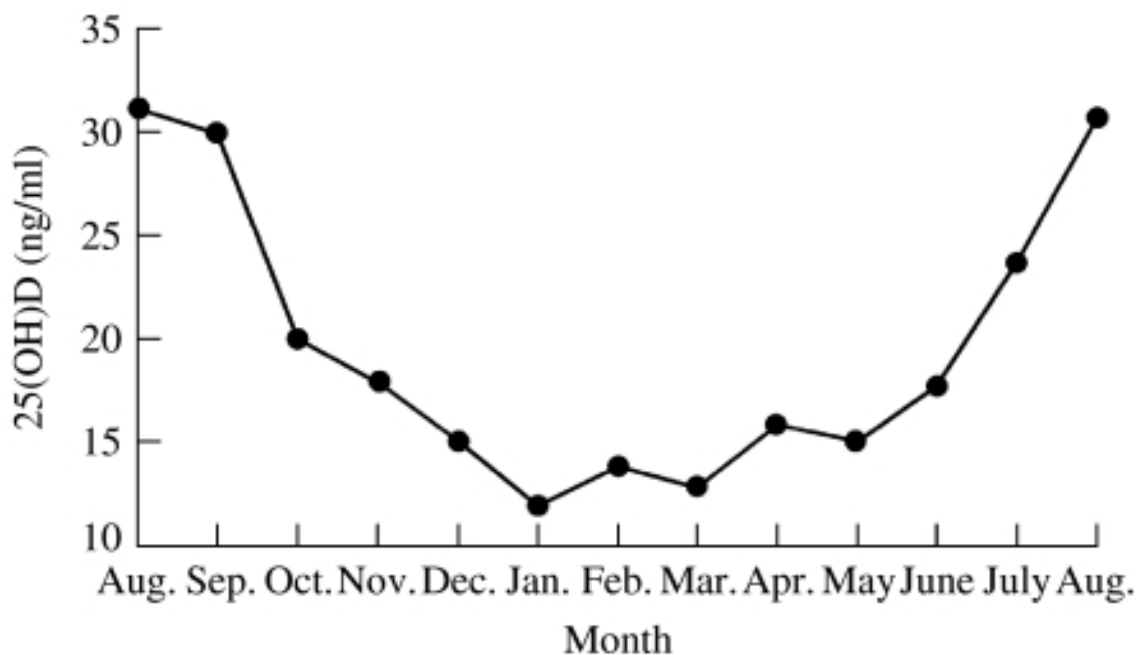


Fig. 3 Seasonal variation of 25(OH)D levels in a population-based sample of inhabitants of a small southern German town, aged 50–80 years. (Reproduced/amended with kind permission of Springer Science and Business Media, Scharla, S.H., 1998.)

[Epidemic influenza and vitamin D](#) Epidemiol Infect. 2006 Dec;134(6):1129-1140.

CORONA VIRUS ABSTRACTS

January, 2020

[N Engl J Med](#). 2020 Jan 24. doi: 10.1056/NEJMoa2001017. [Epub ahead of print]

A Novel Coronavirus from Patients with Pneumonia in China, 2019.

[Zhu N¹](#), [Zhang D¹](#), [Wang W¹](#), [Li X¹](#), [Yang B¹](#), [Song J¹](#), [Zhao X¹](#), [Huang B¹](#), [Shi W¹](#), [Lu R¹](#), [Niu P¹](#), [Zhan F¹](#), [Ma X¹](#), [Wang D¹](#), [Xu W¹](#), [Wu G¹](#), [Gao GF¹](#), [Tan W¹](#); [China Novel Coronavirus Investigating and Research Team](#).

Author information

Abstract

In December 2019, a cluster of patients with pneumonia of unknown cause was linked to a seafood wholesale market in Wuhan, China. A previously unknown betacoronavirus was discovered through the use of unbiased sequencing in samples from patients with pneumonia. Human airway epithelial cells were used to isolate a novel coronavirus, named 2019-nCoV, which formed another clade within the subgenus sarbecovirus, Orthocoronavirinae subfamily. Different from both MERS-CoV and SARS-CoV, 2019-nCoV is the seventh member of the family of coronaviruses that infect humans. Enhanced surveillance and further investigation are ongoing. (Funded by the National Key Research and Development Program of China and the National Major Project for Control and Prevention of Infectious Disease in China.).

[Respirology](#). 2018 Feb;23(2):130-137. doi: 10.1111/resp.13196. Epub 2017 Oct 20.

MERS, SARS and other coronaviruses as causes of pneumonia.

[Yin Y¹](#), [Wunderink RG²](#).

Author information

Abstract

Human coronaviruses (HCoVs) have been considered to be relatively harmless respiratory pathogens in the past. However, after the outbreak of the severe acute respiratory syndrome (SARS) and emergence of the Middle East respiratory syndrome (MERS), HCoVs have received worldwide attention as important pathogens in respiratory tract infection. This review focuses on the epidemiology, pathogenesis and clinical characteristics among SARS-coronaviruses (CoV), MERS-CoV and other HCoV infections.

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[Dermatoendocrinol](#). 2009 Jul;1(4):215-9.

The possible roles of solar ultraviolet-B radiation and vitamin D in reducing case-fatality rates from the 1918-1919 influenza pandemic in the United States.

[Grant WB](#), [Giovannucci E](#).

Abstract

Deaths during the 1918-1919 influenza pandemic have been linked to both the influenza virus and secondary bacterial lung infections. Case fatality rates and percentage of influenza cases complicated by pneumonia were available from survey data for twelve United States locations in the 1918-1919 pandemic. This study analyzes case fatality rates and cases complicated by pneumonia with respect to estimated summertime and wintertime solar ultraviolet-B (UVB) doses as indicators of population mean vitamin D status. Substantial correlations were found for associations of July UVB dose with case fatality rates ($r = -0.72$, $p = 0.009$) and rates of pneumonia as a complication of influenza ($r = -0.77$, $p =$

0.005). Similar results were found for wintertime UVB. Vitamin D upregulates production of human cathelicidin, LL-37, which has both antimicrobial and antiendotoxin activities. Vitamin D also reduces the production of proinflammatory cytokines, which could also explain some of the benefit of vitamin D since H1N1 infection gives rise to a cytokine storm. The potential role of vitamin D status in reducing secondary bacterial infections and loss of life in pandemic influenza requires further evaluation.

[Z Gerontol Geriatr](#). 2018 Jun;51(4):435-439. doi: 10.1007/s00391-017-1237-z. Epub 2017 May 5.

Link between community-acquired pneumonia and vitamin D levels in older patients.

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[Author information](#)

Abstract

PURPOSE:

To investigate the correlation between the level of 25-hydroxyvitamin D [25-(OH)D] and community-acquired pneumonia (CAP) in elderly patients.

METHODS:

A total of 163 older patients were chosen from those hospitalized between October 2011 and October 2012. Patients were divided into pneumonia and non-pneumonia groups, and the concentrations of 25-(OH)D (nmol/L) in serum were measured. Clinical data were then compared between the two groups and pneumonia-related risk factors were analyzed using logistic regression.

RESULTS:

Among the 163 older hospitalized patients, 49 suffered from pneumonia. Levels of 25-(OH)D, total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) were lower ($P < 0.05$) in the pneumonia group, while severe vitamin D (VitD) deficiency was higher in the pneumonia group (71.4 vs. 19.3%; $P < 0.0001$). Age and number of hospitalization days were higher in the pneumonia group ($P < 0.05$). Multivariate logistic regression showed that age and VitD levels were independent risk factors for pneumonia. No significant difference was observed in terms of gender, onset season, body mass index, or smoking and drinking history between the two groups ($P > 0.05$).

CONCLUSION:

The older patients with CAP had a severe VitD deficiency, indicating that low levels of VitD might play an important role in the occurrence and development of CAP.

[Medicine \(Baltimore\)](#). 2019 Sep;98(38):e17252. doi: 10.1097/MD.00000000000017252.

The association between vitamin D deficiency and community-acquired pneumonia: A meta-analysis of observational studies.

[Zhou YF¹](#), [Luo BA²](#), [Qin LL³](#).

[Author information](#)

Abstract

Emerging evidence has shown that vitamin D deficiency may be related with community-acquired pneumonia (CAP), but individually published studies showed inconclusive results. The aim of this study was to quantitatively summarize the association between vitamin D and the CAP. We conducted this meta-analysis through a systematic literature search of PubMed, Medline, and EMBASE up to 31 September 2018 with the following keywords 'vitamin D' or 'cholecalciferol' or '25-hydroxyvitamin D' or '25(OH)D' in combination with 'community-acquired pneumonia' or 'CAP' or 'pneumonia' with no limitations. This meta-analysis was performed following the guidelines of Meta-analysis of Observational Studies in Epidemiology. The association between vitamin D levels and CAP were measured as odds ratio (OR) and weighted mean difference (WMD). Results were combined using a random-effect or a fix-effect meta-analysis, and sensitivity analyses were conducted to explore potential factors. Eight observational studies involving 20,966 subjects were included. In this meta-analysis, CAP patients with vitamin D deficiency (serum 25(OH)D levels < 20 ng/mL) experienced a significantly increased risk of CAP (odds ratio (OR) = 1.64, 95% confidence intervals (CI): 1.00, 2.67), and an obvious decrease of -5.63 ng/mL (95% CI: -9.11 , -2.14) in serum vitamin D was demonstrated in CAP patients. Sensitivity analysis showed that exclusion of any single study did not materially alter the overall combined effect. The evidence from this meta-analysis indicates an association between vitamin D deficiency and an increased risk of CAP patients. However, well-designed trials are required to determine the explicit effect of vitamin D supplementation.

Effect of adjunctive single high-dose vitamin D₃ on outcome of community-acquired pneumonia in hospitalised adults: The VIDCAPS randomised controlled trial.

[Slow S](#)¹, [Epton M](#)², [Storer M](#)², [Thiessen R](#)³, [Lim S](#)³, [Wong J](#)^{4,5}, [Chin P](#)^{4,6}, [Tovaranonte P](#)^{4,7}, [Pearson J](#)⁸, [Chambers ST](#)⁸, [Murdoch DR](#)⁸; VIDCAPS Group.

[Collaborators \(12\)](#)

[Author information](#)

Abstract

Low vitamin D status is associated with increased risk of pneumonia, greater disease severity and poorer outcome. However, no trials have examined the effect of adjunctive vitamin D therapy on outcomes in adults with community-acquired pneumonia (CAP). We conducted a randomised, double-blind, placebo-controlled trial examining the effects of adjunctive vitamin D in adults hospitalised with CAP. Participants were randomised to either a single oral dose of 200,000 IU vitamin D₃ or placebo. The primary outcome was the complete resolution of chest radiograph infiltrate at 6 weeks post-study treatment. Secondary outcomes included length of hospital stay, intensive care admission and return to normal activity. Only participants who completed the study or died within the 6 week period were included in the analysis (n = 60 vitamin D, n = 57 placebo). Adjunctive vitamin D did not have any effect on the primary outcome (OR 0.78, 95% CI 0.31 to 1.86, p = 0.548). However, there was evidence it increased the complete resolution of pneumonia in participants with baseline vitamin D levels <25 nmol/L (OR 17.0, 95% CI 1.40-549.45, P = 0.043), but this did not reach statistical significance using exact methods (OR 13.0, 95%CI 0.7-960.4, P = 0.083). There were no significant effects for any secondary outcome.

PMID:

[Clin Respir J](#). 2018 Jul;12(7):2220-2227. doi: 10.1111/crj.12792. Epub 2018 Apr 16.

Serum 25-hydroxyvitamin D levels in hospitalized adults with community-acquired pneumonia.

[Brance ML](#)^{1,2}, [Miljevic JN](#)³, [Tizziani R](#)⁴, [Taberna ME](#)⁴, [Grossi GP](#)⁵, [Toni P](#)⁵, [Valentini E](#)⁶, [Trepatt A](#)⁶, [Zaccardi J](#)⁷, [Moro J](#)⁷, [Finuci Curi B](#)⁸, [Tamagnone N](#)⁸, [Ramirez M](#)⁹, [Severini J](#)³, [Chiarotti P](#)³, [Consiglio F](#)¹⁰, [Piñeski R](#)¹⁰, [Ghelfi A](#)¹¹, [Kilstein J](#)¹¹, [Street E](#)¹², [Moretti D](#)¹³, [Oliveto V](#)¹⁴, [Mariño M](#)¹⁵, [Manera J](#)¹⁵, [Brun LR](#)^{1,2}.

[Author information](#)

Abstract

INTRODUCTION:

Community-acquired pneumonia (CAP) is the infectious disease with the highest number of deaths worldwide. Several studies have shown an association between vitamin D deficiency and increases susceptibility to respiratory tract infections.

OBJECTIVE:

The aim of this study was to evaluate the serum 25-hydroxyvitamin D (25OHD) levels in hospitalized adults in general room with CAP.

MATERIALS AND METHODS:

An observational study was carried out in 207 hospitalized adults of both sex with CAP (>18 years) from Rosario city, Argentina (32° 52' 18"S) between July 2015 and June 2016.

RESULTS:

In total, 167 patients were included in the data analysis [59% women (57.4 ± 19.6 years), body mass index 27.2 ± 7.8 kg/m²]. In brief, 63% showed unilobar infiltrate and 37% were multilobar. The CURB-65 index was 66.5% low risk, 16.0% intermediate risk and 17.5% high risk. According to Charlson comorbidity index (CCI) 53.5% had not comorbidity (CCI = 0) and 46.5% showed CCI ≥ 1. The 25OHD level was: 11.92 ± 7.6 ng/mL (51.5%: <10 ng/mL, 33.5%: 10-20 ng/mL, 13.2%: 20-30 ng/mL and 1.8%: >30 ng/mL). Higher 25OHD were found in male (female: 10.8 ± 6.7 ng/mL, male: 13.5 ± 8.5 ng/mL, P = .02) and 25OHD correlated with age (r = -.17; P = .02). 25-Hydroxyvitamin D was also correlated with CURB65 index (r = -.13; P = .049), CCI (r = -.20, P = .007) and with the 10 years of life expectative (%) (r = .19; P = .008). In addition, higher 25OHD were found with lower CCI (CCI 0 = 13.0 ± 8.2 ng/mL, CCI ≥ 1 = 10.5 ± 6.7 ng/mL; P = .0093).

CONCLUSIONS:

Hospitalized adults with CAP have lower 25OHD levels and would be associated with the severity of CAP.

[Int J Gen Med](#). 2017 Nov 13;10:423-429. doi: 10.2147/IJGM.S149049. eCollection 2017.

Association between serum concentration of 25-hydroxyvitamin D and community-acquired pneumonia: a case-control study.

[Mamani M](#)^{1,2}, [Muceli N](#)², [Ghasemi Basir HR](#)³, [Vasheghani M](#)⁴, [Poorolajal J](#)⁵.

Author information**Abstract****BACKGROUND:**

Community-acquired pneumonia (CAP) is a common disease with significant morbidity and mortality. There is evidence that vitamin D deficiency can be associated with infectious diseases. The aim of this study was to compare the levels of vitamin D between patients with CAP and healthy controls.

METHODS:

In a case-control study on 73 patients with CAP and 76 healthy controls, the serum concentration of 25-hydroxyvitamin D (25[OH]D) was measured. Severity and outcomes of disease and also duration of hospital stay were compared in patients with different levels of 25(OH)D. The severity of CAP was assessed using the CURB-65 score (confusion, uremia, respiratory rate, low blood pressure, age ≥ 65 years) and was also reflected by the length of hospital stay, admission to intensive care unit (ICU), and 30-day mortality.

RESULTS:

In total, 81.2% of the study population had vitamin D levels < 30 ng/dL. The risk of pneumonia among subjects with deficient vitamin D levels was 3.69 (95% CI: 1.46, 9.31) times of those with sufficient vitamin D level ($P=0.006$). Prevalence of severe deficiency of vitamin D in scores three and four of CURB-65 (59.38%), was far more than scores one and two (31.71%). Also, results indicated patients with severe deficiency had a higher risk for ICU admission, 30-day mortality, and longer hospitalization stay, but these were not statistically significant.

CONCLUSION:

According to findings, a low level of 25(OH)D is associated with a higher incidence of CAP and more severe disease. It is recommended to pay more attention to vitamin D deficiency in infectious diseases, particularly in CAP patients.