

COVID-19, and Vitamin D, and Air Pollution Global Epidemics Impact on Older Adults

Ray Marks^{1,*}

¹Departments of Health and Behavior Studies, Columbia University, Teachers College, New York, NY, USA 10027.

Abstract

Background: Most current Corona virus or COVID-19 pandemic deaths have been found to occur among populations older than 65 years of age, who often suffer from the presence of an array of chronic diseases that may be related to a co-occurring vitamin D deficiency. Another factor affecting older adults' immune response mechanisms is air quality. In turn, air quality can impact the absorption of vitamin D from sunlight sources, a factor which could explain why older people, who are often vitamin D deficient, may be more likely than younger adults or healthy adults to be at risk for COVID-19 and poor outcomes.

Aim: This work was designed to examine the recent literature on COVID-19, vitamin D and air pollution and what it might imply for public health workers, policy makers, and others.

Methods: Available data accessed largely from the PUBMED data base for the year 2020 using the key words *COVID-19*, *air pollution*, and *vitamin D deficiency* were sought and selected items were carefully examined and documented in narrative and tabular formats.

Results: Many publications on COVID-19 prevail, but far fewer focus specifically on vitamin D deficiency and its possible role in explaining COVID-19 global health risk among older adults. A similar, albeit small number of publications, discuss the global pandemics of air pollution and its possible COVID-19 association, as well as its impact on vitamin D production. However, while most related articles support a possible independent as well as a dual role for both factors in COVID-19 the realm of this highly infectious widespread disease, very few actual studies have been conducted to date on any of these topical issues

Conclusion: More research to examine if vitamin D-based nutrients or supplements may provide some degree of community wide protection against COVID-19 in the older vitamin D populations, especially among those living in highly polluted areas may prove highly valuable. Controlling air pollution emissions globally and locally may also prove to be a highly impactful public health approach to reducing overall COVID-19 risk, and extent, and warrants study.

Corresponding author: Ray Marks, Department of Health and Behavior Studies, Teachers College, Columbia University, Box 114, 525W, 120th Street, New York, NY 10027, United States, Tel.: 1-212-678-3445

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Introduction

As of December 9, 2020, it appears safe to say there is almost no country that has not been affected by the novel Corona virus or COVID-19 infectious disease pandemic, an airborne transmitted infectious disease that emerged in December 2019 in Wuhan, China. In particular, in all cases, it appears Covid-19 infected adults over 65 years of age, no matter where they live, are more likely to be hospitalized, and recover less well, in the event they do, when compared to younger adults and children [1]. A disease associated largely with symptoms of distress of the respiratory system, that is often associated with the presence of pre-existing co-morbid health conditions such as cardiovascular disease, diabetes and obesity, the presence of any of these age-associated health conditions may place the older adult at high risk for this condition, as well as for poor outcomes among survivors. But this explanation alone does not seem to help explain why COVID-19 disease does not present in a uniform manner among all older adults, including healthy older adults, as well as those with one or more underlying health conditions [1].

Since there is no present vaccine that is widely available, and COVID-19 outbreaks are clearly spreading rapidly in many regions that are home to populations that are aging, it appears of high import to continue to uncover any tentative explanations as to why COVID-19 tends to occur at high rates in the elderly, who are increasing in numbers globally as populations age. It is also acknowledged that even if vaccines found effective are available to all, older adults may not respond as well as younger adults to these, thus multiple effective approaches to minimizing the risk of this novel lethal respiratory condition is not only

warranted, but urgent. In addition, not all countries will have vaccine access in the near future, hence cost effective safe efficient ways to curb any future COVID-19 outbreak, and reduce the need for hospitalizations or long-hospital stays are especially desirable. In this regard, this present narrative report was designed to share what is known, and the experiences and insights of scientists in the field as regards two overlapping or parallel factors that appear valuable for persons in the public health field to study, namely air pollution, and the implication of vitamin D deficiencies, which exist worldwide

Unfortunately, since it is but a year since COVID-19 became problematic, well-established definitive research studies are clearly not available, thus this report relies on preclinical or previously conducted research to some degree, or viewpoints of experts, plus the voices of concerned scientists.

Aim

This current review aims to document key facts about two factors that may independently or collectively contribute to COVID-19 risk among older adults, namely vitamin D deficiency and air pollution. It also aims to summarize what experts suggest should be done currently, as well as in the future in both research and practice, mindful, these factors are not the only factors warranting examination, but both are widespread preventable factors.

Exploratory Hypothesis

The exploratory hypothesis tested in this mini review is that air pollution, as well as vitamin D deficits are co-occurring global epidemics that warrant attention in the fight to prevent or eliminate the risk of COVID-19, regardless of any future vaccine.

Materials and Methods

The PUBMED electronic data and others, such as SCOPUS, Web of Science, and Google Scholar were used to search for relevant information published in 2020 using the key terms presented in Table 1. Some data that were observed to be relevant from the references used in several reports were also sought and documented. Only English language based articles or available abstracts on vitamin D deficiency, air pollution, and COVID-19 among older adults were sought and examined. All forms of publication were deemed acceptable.

Relevant data were carefully examined and those that were deemed appropriate by the author are presented in this paper solely in descriptive terms and according to their relevance regarding the key topics of current concern. Some corresponding data were tabulated as well for ease of reviewing the diverse comments, as well as providing some narrative information of the overlapping ideas and discussion trends, and support or lack of support for the hypothesis being explored.

Articles not sufficiently focused on the specific topics of interest in the present review were excluded. For example, those that referred to children, those that discussed nutrition in general, and those that were theoretical or non-English based studies were excluded. To begin to examine the data perceived to be of salience, the author identified four key categories as per data reviewed below, and the selections presented are purely descriptive, rather than quantitative summaries. Since articles and data bases were selected and

reviewed by the author, it is acknowledged these data may not represent all thematic perspectives, or articles in data bases not searched.

Results

General Findings

Table 1 below details the relative numbers of publications on topics embedded in this review as of mid November 2020.

Results of the search further revealed that despite the considerable number of publications listed at PUBMED as cited in Table 1, only very few articles relevant to this review were found as a whole, even when other data bases were searched. That is, when the entire spectrum of the listed publications was examined within each search term, very limited numbers of pertinent papers addressing the themes of this ensuing discourse could be located. This is because, there were many articles that were very broad commentaries, rather than explicit reviews or empirical based reports, possibly because this is a novel field of exploration and inquiry. Moreover, among those publications deemed relevant, it was clearly impossible to aggregate such a diverse array of publication themes and modes of inquiry that were organized at the data base sites in any effective systematic way.

Specific Findings

Prevalence and Disease Burden of COVID-19

Despite the interest in COVID-19, which is clearly immense when viewing PUBMED for 2020 as shown in Table 1, precise prevalence data on COVID-19 are not only hard to locate, but appear to be constantly

Table 1. Summary PUBMED articles and main results as of mid-November, 2020

Key terms	Numbers	Main Types Reports	No. Clinical Trials
COVID-19	75554	8150 reviews	195
COVID-19 + Older Adults	8421	86 reviews	2
COVID-19 + Vitamin D	284	6 reviews	2
COVID-19 + Vitamin D Deficiency	101	2 reviews	0
COVID-19 + Air Pollution	382	2 reviews	0
Air Pollution + Vitamin D	131	5 reviews	2

changing. In this regard, there appears to be more papers discussing exponential increases in COVID-19 prevalence, rather than decreases over the past year. Selected areas across the globe on the other hand, show few or no cases in rare circumstances as of mid November 30 2020. Others report better success at limiting widespread infections than others. Most cases to date have however, been elderly adults, with or without pre-existing health conditions, regardless of country examined. At the same time, possible additional determinants of COVID-19 risk or susceptibility examined at this time include air pollution, a variety of nutritional factors, and low socioeconomic status. Most data emanate from already infected adults, and thus what is known may be limited to an already impaired elderly subgroup. Data show however, there may be a total of 60 predictors for disease severity, of which seven appear to be highly consistent, while 40 are said to be of medium relevance, and 13 of low relevance. Among those factors that tend to occur with associated consistency other than age are, C-reactive protein levels [a marker of inflammation], D-dimer presence – a prognostic marker released when a blood clot breaks down, albumin, body temperature, a SOFA [sepsis related] score and diabetes [2].

These data stress the need to focus on the elderly, especially those with possible underlying inflammatory, chronic, cardiac and respiratory conditions that may precipitate COVID-19 risk and lethality, and may in turn heighten pre-existing disease symptoms that may be associated in their own right with remediable determining factors [3-5]. These include vitamin D and its impact on innate immunity, as well as the impact of poor air quality, negative health behaviors, and various degrees of mental health status [6-10].

Vitamin D and its Global Impact on Health

While the skeletal and extra skeletal effects of vitamin D have been described and studied for some time, more recent work shows vitamin D to have widespread effects on gene expression, as well as overall health. In the context of respiratory infections such as COVID-19, additional research shows vitamin D can serve to provide a key barrier function within the lining of the respiratory tract. It can also

play an essential role in immune system functioning [11]. Alternately, a vitamin D deficiency has the potential to increase mortality rates in the elderly with cardiovascular diseases, and various forms of cancer, who often exhibit high rates of vitamin D deficiency, and who are highly susceptible to COVID-19 infections. Vitamin D also has important innate antimicrobial properties [12] that may explain its proposed role in the context of COVID-19 disease [13, 14].

At the same time, vitamin D production in the skin, which is known to decline with advancing age, possibly renders older populations more dependent on dietary vitamin D than younger populations, in the event of poor air quality or lack of sunlight exposure or both, among other factors. However, this may go undetected, and hence untreated, and thus it is no surprise that vitamin D deficiency is common among older adults in all parts of the world [15], even in sunny climates, where it may predict an older adults' increased risk of incurring a COVID-19 infection [16].

A vitamin D deficiency has also been found to occur more frequently in adults with diabetes, a leading predictor of COVID-19 severity [17, 18].

On the other hand, since vitamin D presence is found to decrease the lethality of acute respiratory infections similar to those occurring in persons with COVID-19 infections. COVID-19, it has been suggested that COVID-19 infections may be impacted favorably by efforts to rectify any prevailing hypovitamin D levels among vulnerable adults [19-21], especially adults with coexisting diabetes [22]. Bielkoski et al. [23] further supports this view given the past evidence for a role of vitamin D deficiency in respiratory tract infections that are more frequent in the winter months and especially in the northern latitudes than they are in summer. Moreover, a low vitamin D status, measured as the plasma level of the transport form of vitamin D, 25(OH) D is widespread worldwide. Table 2.

Air Pollution and COVID-19

Pollution, an under-reported possible mediator or moderator of COVID-19 including air pollution, is associated with various forms of allergy, as well as influencing the extent of autoimmunity [33]. In addition, empirical evidence supports an important role for air

Table 2. Sample of available reports on vitamin D and COVID-19 and their conclusions

Author	Tentative Conclusions
Ali [24]	Adults at high risk of vitamin D deficiency during this global pandemic should consider taking vitamin D supplements to maintain desirable and optimal levels
Backtash et al. [25]	Older adults with vitamin D deficiency and COVID-19 may demonstrate worse morbidity outcomes. Vitamin D status may be a useful prognosticator
Grant et al. [21]	People infected with COVID-19 may benefit from Vitamin D
Hastie et al. [26]*	Findings do not support a link between vitamin D concentrations and risk of COVID-19
Ilie et al. [27]	Performing dedicated studies about vitamin D levels in COVID-19 patients with different degrees of disease appears warranted
Mohan et al. [28]	There is ecological and mechanistic support for promoting exploration of vitamin D action in COVID-19 patients
Mitchell [29]	A role for vitamin D relative to COVID-19 is indicated due to its role in the production of antimicrobial peptides in the respiratory tissues as well as its inflammatory impact on infection
Rajudkovic et al. [30]*	There is an association between vitamin D deficiency and COVID-19 severity
Riberio et al. [31]	Adequate vitamin D status may play a role in prevention and management of respiratory tract infections such as COVID-19
Roy et al. [17]	Well-designed randomized controlled trials may reveal the efficacy of vitamin D as an adjuvant therapy for COVID-19
Weir et al. [18]	Vitamin D deficiency is associated with an increase in thrombotic episodes
Xu et al. [32]	Vitamin D supplementation can reduce the risk of COVID-19 incidence and severity

pollution in the accelerated transmission of COVID-19, as seen in Italy, as well as in Wuhan, China. Lockdown-related reductions in selected air pollution indicators have conversely contributed to reduced transmission of the virus, while high levels of particulate matter or microorganisms in the air as a result of excess air pollution might have initially accelerated COVID-19 transmission and risk or continue to add to COVID-19 related mortality rates. Hence, post-lockdown increases in pollution may again accelerate COVID-19 transmission as well as adding to the burden of COVID-19 morbidity and mortality [34].

Research further implies that COVID-19 is largely transmitted by air and the presence in the air of certain forms of atmospheric particulate matter potentially create a suitable environment for transporting the virus at greater distances than those considered for close contact. Moreover, particulate matter is said to induce lung cell inflammation and this could increase the susceptibility and severity of the COVID-19 related symptoms. In Italian cities for example, retrospective data show particulate matter daily concentrations were higher than the annual average in the months preceding the COVID-19 pandemic [35].

In a systematic review on this issue, it was concluded however, that as a whole, this association, is hard to validate because researchers often use different research methods or do not include confounding factors into their analyses. In addition, to date incidence data are possibly underestimated in all countries and to a lesser extent the same applies to mortality data. For this reason, the cases included in the reviewed studies could not be considered conclusive, but major findings are tentatively consistent as regards the importance contribution of selected air pollutants to trigger the spread of COVID-19. These pollutants also tend to increase lethality [36].

Air Pollution and low Vitamin D Status

As outlined above, exposure to chronic levels of air pollutants currently constitutes a widespread human and global health risk [35]. At the same time, the synthesis of vitamin D in human skin due to sun exposure may be reduced by air pollution causing a possible vitamin D deficiency [35]. Prospective and

observational studies confirm populations living in different geographic areas may show an increased prevalence of a low vitamin D status in the presence of air pollution [35]. According to others, one possible reason for the high rates of vitamin D deficiency is the presence of high levels of air pollution, as air pollution might block those ultraviolet rays that need to be absorbed by the skin and translated into active vitamin D [37, 38]. Ritu et al. [39] similarly note that atmospheric pollution even in metropolitan India, which is otherwise sunny, potentially impacts vitamin D status adversely. He He et al. [40], similarly note that a vitamin D deficiency is common in sub-tropical locations, such as the Sichuan Basin, which is related to solar radiation and air pollution, rather than climatic conditions. Reasons for concern according to these authors and others are the following:

High levels of air pollution affect the body's natural defenses against airborne viruses, increasing the likelihood that people will contract viral diseases, such as COVID-19, especially those who are vitamin D deficient.

Exposure to air pollution increases the risk for many of the chronic diseases that are often linked to vitamin D deficits, and tend to render people more likely to develop serious illnesses requiring intensive care and mechanical ventilation due to COVID-19.

Exposure to air pollution can worsen symptoms of respiratory infections, while increasing the risk of hospitalization and death [41-43]

Discussion

COVID-19, now prevalent in more than 180 countries, shows no sign of abating. At the same time, vaccine development is not yet a viable solution for the present. On the other hand, remediable upstream as well as pervasive downstream factors that may be associated with the risk of acquiring a COVID-19 infection and its often negative outcomes are highly sought as a result. This commentary sought to examine the idea that a pervasive vitamin D deficiency found to be occurring at high rates all over the world, including countries in the southern hemisphere, may be one such factor. It further explored the possible impact of air pollution on COVID-19 risk, as well as vitamin D

deficiency. The rationale for this choice is that all three of these situations predominantly affect the health of older persons, along with persons of color and low socioeconomic status. [44].

In addition, a sizeable volume of past research shows vitamin D is needed to protect viral infections due to its impact on the immune system [45]. In turn, air pollution can not only diminish vitamin D sunlight sources, but act as a viral carrier and immune system pathogen in its own right.

In this regard, Benskin [46] reported that the innate immune system, if impaired by a vitamin D deficiency, could predispose sufferers to viral infections such as COVID-19. Vitamin D deficiency also increases the activity of the X-chromosome-linked "Renin-Angiotensin" System, making vitamin D deficient individuals (especially men) more susceptible to COVID-19's deadly "cytokine storm", which is a dramatic overreaction of the immune system. Another finding is that the groups at highest risk for severe COVID-19 are those at highest risk for severe vitamin D deficiency, including the elderly, men, ethnic groups whose skin is naturally rich in melanin (if living outside the tropics), those who avoid sun exposure for cultural and health reasons, those who live in institutions, the obese, and/or those who suffer with hypertension, cardiovascular disease, or diabetes. Another observation is that the pattern of geographical spread of COVID-19 reflects higher population vitamin D deficiency patterns, and both within the US and throughout the world, COVID-19 fatality rates parallel vitamin D deficiency rates [46].

While regular sunlight exposure is a preventive measure against vitamin D deficiency and can prevent diseases related to it, the urban population, especially the older one, tends to be less exposed to sunlight, due to many factors. One of these might be air pollution. Others may be lack of spaces with gardens, open windows or balconies. At the same time, the quality of air alone may either raise the risk of COVID-19 or help to reduce the risk, especially among vulnerable older adults [48, 49].

As based on current data, the present working hypothesis, while limited by the lack of adequate research, would in our view thus tend to support, rather

than refute the idea of a possible clinically relevant linkage between air pollution, and vitamin D deficiency and COVID-19 among the elderly that warrants attention [12, 31, 48, 49]. In addition, efforts to maximize vitamin D serum levels, while ensuring air pollution is kept to a minimum, and does not impact adversely on COVID-19 prevalence and fatality rates as a result of its ability to increase susceptibility to bacteria and viruses in the respiratory system appear especially relevant among adults with pre existing health conditions [43, 29, 50, 51].

Indeed – in the absence of a vaccine, and given that air pollution will possibly tend to increase as social distancing rules are relaxed, society should be urged to remain vigilant about limiting air pollution, especially since the virus can survive for a longer period when attached to a pollutant [48].

Conclusions

This review demonstrates the need to be vigilant as regards air pollution and its role in fostering airborne transmission of COVID-19, while acting as a sunlight deterrent to vitamin D skin absorption that is needed to promote immune functions, and reduce infection risk.

Despite the lack of clinical trials, the review demonstrates efforts to maximize vitamin D levels among older vulnerable adults, along with efforts to minimize air pollution globally and locally warrants immediate attention and concerted action to counter these independent epidemics.

Public health workers can serve in many ways in this regard by advocating for policies and funding to secure harm reduction efforts in both these spheres and can in our view use current data to ably support their arguments to protect the older COVID-19 susceptible adult until additional data are forthcoming.

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Conflicts of Interest

"The author declares no conflict of interest."

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