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Worsening air pollution an unfamiliar cause of low vitamin d levels: A systematic literature review

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Abstract

Air pollution is widely recognized as a future biohazard, yet its direct effects on human health, particularly in relation to bone health and vitamin D levels, are inadequately understood. While the detrimental impact on respiratory and cardiovascular health is well-documented, the correlation with vitamin D deficiency remains weak.

To explore the relationship between air pollution and vitamin D levels, an extensive search of scientific literature was conducted. This comprehensive search encompassed databases such as PubMed, Cochrane Library, and DOAJ, while also examining the bibliographies of relevant articles. The inclusion criteria focused on studies that specifically investigated the association between air pollution and vitamin D levels, while excluding systematic reviews, case reports, editor's letters, and studies lacking pertinent explanations or causative factors. Each included study underwent rigorous evaluation of its methodological quality, with data extraction performed to assess the reliability and robustness of the evidence for each research question.

The majority of studies have consistently demonstrated a negative correlation between ambient air pollution and vitamin D levels in humans. Several mechanisms have been proposed to explain this relationship, including reduced exposure to sunlight due to increased air pollution, production of reactive oxygen particles, and inflammation leading to decreased vitamin D synthesis. Moreover, certain pollutants, such as particulate matter and nitrogen dioxide, have been found to have a more pronounced impact on vitamin D levels. Variables such as age, gender, season, and geographical location may also influence the association between air pollution and vitamin D levels. Lifestyle factors, including indoor confinement and pre-existing vitamin D deficiency, may exacerbate the detrimental effects of air pollution.

In conclusion, air pollution detrimentally affects vitamin D levels primarily through increased body inflammation and the generation of free radicals. The presence of elevated levels of particulate matter and nitrogen dioxide further compounds this effect. Additionally, decreased cutaneous production of activated vitamin D, resulting from reduced ultraviolet B radiation penetration due to decreased Air Quality Index, contributes to the negative impact. Studies suggest that the intake of exogenous vitamin D supplements and adherence to a calcium-rich diet may confer benefits to individuals residing in highly polluted areas. To address this issue, public health policies should emphasize outdoor exposure to sunlight, promote healthy dietary choices, and reduce overall exposure to pollutants.

Key words: air pollution, vitamin D levels, dietary supplements, and free radicals

Introduction

The activated form of vitamin D plays a crucial role in the musculoskeletal system. It influences bone health by promoting the absorption of calcium and phosphorus from the intestine, maintaining calcium balance through the kidney, and regulating the release of parathyroid hormone [1].

Vitamin D deficiency can lead to decreased bone mineral density, osteomalacia, and an increased risk of fractures, making it particularly concerning during childhood and adolescence when skeletal growth and development are critical [2, 3, 4]. Additionally, vitamin D is essential for immune regulation and cell growth [5].

Interestingly, the activated form of vitamin D is expressed in various tissues, including neurons, glial cells, epithelial cells, prostate cells, keratinocytes, and macrophages. This local expression contributes to the regulation of genes involved in cell proliferation and differentiation [6]. Epidemiological evidence suggests that vitamin D deficiency is linked to the pathogenesis and progression of chronic diseases and autoimmune disorders, such as cancer, multiple sclerosis, and rheumatoid arthritis [7].

In pregnant women, vitamin D insufficiency has been associated with pre-eclampsia, gestational diabetes mellitus, fetal development limitations, and preterm birth [8]. The primary sources of vitamin D for humans are sunlight exposure and dietary consumption [9].

While there is no consensus on the precise levels that define vitamin D deficiency and sufficiency, a level of 30nmol/L is generally considered protective of bone health, with levels below this considered insufficient. Studies have also classified serum 25(OH) D levels of 20 ng/ml as deficiency, 20 to 30 ng/ml as insufficiency, 30 to 60 ng/ml as sufficiency, and >150 ng/ml as intoxication [1].

Vitamin D deficiency is recognized as a global health concern [10]. Although the exact global burden of vitamin D deficiency is uncertain, research suggests that it is prevalent in many countries, particularly in the Middle East, India, China, and Mongolia [11]. For instance, studies have reported high prevalence rates of vitamin D deficiency in India (61%), Iran (86%), and Turkey (51%) [12].

In recent years, urban areas have experienced an increase in air pollution, primarily from sources such as motor vehicle emissions, industrial combustion, and heating [13]. In 2016, 95% of the world's population resided in regions where ambient particulate matter 2.5 m (PM2.5) levels exceeded the World Health Organization's (WHO) guidelines of 10g/m3 [14]. It is hypothesized that high levels of air pollutants, including ozone, particulate matter PM2.5, and sulfur dioxide, can reduce the cutaneous synthesis of pre-vitamin D3 by effectively absorbing UVB photons [15]. Moreover, high concentrations of air pollutants and dust in the atmosphere reduce visibility and limit exposure to the sun's ultraviolet radiation [16].

Vitamin D deficiency can negatively impact regular inflammatory mediators, potentially harming the skeleton [17]. Furthermore, exposure to high levels of air pollution may increase bone turnover markers, such as osteocalcin and C-terminal telopeptide of type I collagen (CTx) [18].

In this systematic review, we aim to explore the correlation between air pollution and vitamin D deficiency. We will also investigate factors such as race, gender, and age that may influence this correlation, and propose potential solutions to address this issue.

Material and methods

A systematic search was conducted on PubMed, Cochrane Library, and DOAJ using the terms 'Vitamin D' and 'Air Pollution.' References from primary and review articles and major orthopaedic texts were cross-referenced to identify additional reports that met the inclusion criteria but were not identified by the initial search. All articles published up until December 2022, including online articles, were included.

Inclusion requirements

The study included original articles on Vitamin D and Air pollution.

Exclusion criteria

Excluded were systematic reviews, case reports, and letters to the editor. Excluded were studies in which the association was discussed without cause or relevant explanation.

Extraction of data, analysis, and results

The articles included in the study were independently evaluated by two authors. One reviewer extracted the data, which was then reviewed by the second author. Additionally, data were extracted and reviewed independently. Prior to proceeding, disagreements were resolved.

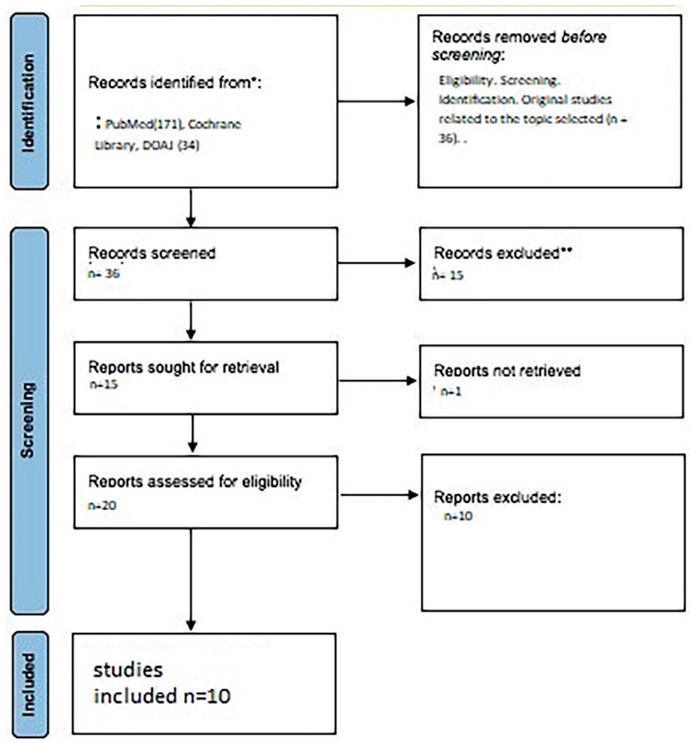

Figure 1 - Identification of studies via databases and registers

The authors then compiled and analyzed the data, attempting to answer the following questions:

1. Is there a connection between vitamin D and ambient air pollution, and if so, what is the nature of this connection?
2. Exist additional factors that influence this relationship and vitamin D levels?
3. How can we avoid this issue?

Results

Research conducted by Feizabad et al. [19] in 2017 suggests that air pollution reduces the amount of UVB radiation reaching the Earth's surface, thereby impacting vitamin D levels. Similarly, He et al. [20] found a negative correlation between air quality index (AQI) and vitamin D levels in China in 2020. Another study by Yan Zhao et al. [21] in China in 2019 revealed that a decrease in daily net radiation mediates the negative association between particulate air pollution (PM10 and PM2.5) and vitamin D levels in expectant women. This study also highlighted that UVB absorption primarily drives this association.

Furthermore, Aggarwal et al. [16] found that children living in areas with higher air pollution levels had a higher incidence of vitamin D deficiency, rickets, and elevated levels of PTH and ALP. They indirectly measured the reduced amount of UVB radiation reaching the Earth's surface in more polluted regions using haze sensors.

In a study comparing the vitamin D status of healthy women aged 20 to 55 in Tehran (a more polluted area) and Ghazvinian (a less polluted area), Farhad Hosseinpanah et al. observed that ground UVB radiation, measured using a haze meter, served as a proxy for air pollution. The study showed that the mean standard deviation of serum 25-hydroxy vitamin D was significantly higher in Ghazvinian women (18±11) compared to Tehranian women (13±7). The prevalence of vitamin D levels below 10 ng/ml and between 10 and 20 ng/ml was higher in the Tehranian group (36% and 54%) compared to the American group (31% and 32%). Additionally, secondary hyperparathyroidism was more prevalent among Tehranian women (47% vs. 32%) [4].

Manicourt DH conducted a Belgian study in 2008 involving postmenopausal women, where urban tropospheric ozone levels were used as a proxy for air pollution as it is the most common urban air pollutant and absorbs solar radiation. The study revealed that urban tropospheric ozone levels were three times higher than rural levels (80.4±18.2 g/m3 versus 27±10 g/m3). Despite urban residents having nearly 1.3 times more sun exposure than rural residents, more urban residents had insufficient vitamin D levels (32 out of 38 versus 18 out of 47 with 25-hydroxyvitamin D ≥ 75 nmol) [22].

A pilot investigation by Calderón-Garcidueas L et al. [23] involved 20 children from Mexico City and 15 controls. The study found that 6-year-olds in Mexico City had higher IL-6 levels, vitamin D deficiency, and spent less time outdoors. However, it is worth noting that adolescents in more polluted areas tend to spend less time outdoors, which could be a confounding variable. Their investigations in Mexico City showed that lifelong exposure to a polluted environment, including above-standard concentrations of particulate matter 2.5, is associated with significant systemic inflammation and immune dysregulation. There are further studies like the studies by Minna Pekkinen et al that emphasize that in adolescents with similar dietary intake and similar physical activity level the vitamin D levels and BMD levels can vary hence the association with other factors like air pollution need to be evaluated [24-27].

In a cross-sectional study of 100 children, Roya Kelishadi et al. [28] discovered an independent inverse association between Air Quality Index and 25-hydroxy (OH) vitamin D levels. This finding explains the high prevalence of vitamin D deficiency among infants in Isfahan, Iran. The study concluded that the dietary vitamin D intake alone could not account for the extremely low serum 25(OH)D levels. As a result, air pollution should be considered a contributing factor to the etiology of hypovitaminosis D in regions with abundant sunlight.

In a study involving 375 mothers in France, Nour Baz et al. [29] used the atmospheric dispersion modelling system (ADMS-Urban) pollution model, which combined data on traffic conditions, topography, meteorology, and background pollution at the mother's home address to asses particulate matter less than 10 µm in diameter and nitrogen dioxide during pregnancy. Cord blood samples were then collected at birth and were analyzed for levels of 25(OH)D. It was found that maternal exposure to ambient urban levels of Nitrogen Dioxide (NO2) and PM10 strongly predicted low vitamin D status in infants. The correlation was particularly significant during the third trimester. The associations were significant in almost every trimester of gestation but were strongest for the last trimester exposure window. The impact of air pollution exposure during the last trimester of gestation is all the more important because maternal supply of vitamin D declines gradually in pregnancy and reaches its lowest level in the third trimester. Their observation that cord blood serum 25(OH)D concentration varied with the seasons higher levels in summer when sun exposure is the highest as compared to other seasons and then their d model was adjusted for this parameter.

However, a review article by M. Barati et al. [30], which analyzed 35 articles, found no association between the prevalence of vitamin D deficiency and various air pollution parameters, including the number of days with reduced visibility due to dust.

Taken together, these studies demonstrate a correlation between air pollution and diminished vitamin D levels, potentially leading to vitamin D deficiency and rickets in children. Air pollution reduces the amount of UVB radiation reaching the Earth's surface, which primarily contributes to this relationship. Regions with higher air pollution levels also tend to have a higher prevalence of vitamin D deficiency. Additionally, expectant women exposed to NO2 and PM10 are more likely to give birth to infants with low vitamin D levels.

In a 2017 investigation conducted by Elham Feizabad and colleagues, the focus was primarily on adolescents (325 middle and high school students were studied). During the study period, detailed daily data on air pollution were obtained from archived data collected by Tehran Air Quality Control Company (AQCC). Serum levels of calcium, phosphorus, parathyroid hormone (PTH), bone-specific alkaline phosphatase, 25(OH) vitamin D, osteocalcin, cross-linked C-telopeptide (CTX), total protein, albumin, and creatinine were obtained from the study group. The study observed that males had higher levels of vitamin D in both polluted and unpolluted areas, while the prevalence of vitamin D deficiency was twice as common in girls. However, the difference in vitamin D levels between polluted and unpolluted areas was significantly greater in males, suggesting that they are more susceptible to the effects of air pollution (55.7.1 vs 9%), serum vitamin D levels in the polluted area were significantly lower than levels in the non-polluted area (22.4±1.23 ng/ml vs 34.25±1.71 ng/ ml) [19].

A 2020 study conducted in China by He et al. revealed that in subtropical regions, young people and females tended to have lower levels of vitamin D despite similar environmental conditions [20]. For younger age groups, even though their vitamin D intake was higher, the prevalence of vitamin D deficiency remained high due to spending less time outdoors and more time indoors. Other studies have also suggested that excluding the elderly population from taking supplements would lead to an even higher prevalence of vitamin D deficiency [31]. In females, the use of sunscreen and cosmetics contributed to reduced UV exposure, while the prevalence of vitamin D deficiency was lower in the summer [20, 32].

In a study published in China in 2019 by Yan Zhao et al. [21], it was found that exposure to particulate air pollution during the third trimester of pregnancy had a greater impact on vitamin D status. Similar results were observed in a French study by Nour Baz et al. [29]. Since 80% of intrauterine bone mineralization occurs during the third trimester and vitamin D plays a crucial role in this process [33], the fetal demand for vitamin D increases, potentially leading to vitamin D depletion in the maternal blood supply [34]. Therefore, there is a need for vitamin D supplementation during the third trimester, especially in polluted areas.

In a study conducted in Tehran in 2017, Feizabad discovered that adolescents with calcium intakes exceeding 5,000 mg per week showed significant improvements in markers of bone turnover [19]. A study by Agarwal et al. [16] recommended administering a single, large dose of oral vitamin D supplementation at the beginning of winter to protect infants from vitamin D deficiency.

A pilot study conducted on six-year-olds in Mexico City by Calderón-Garcidueas et al. [23] concluded that pediatricians should evaluate the bone health of children living in highly polluted megacities and communities with high levels of particulate matter, taking into account systemic inflammation and deficiencies in vitamin D and calcium in the diet.

Conclusion

Air pollution negatively impacts vitamin D levels primarily due to increased body inflammation, elevated levels of particulate matter nitrogen dioxide, and reduced production of activated vitamin D in the skin as a result of decreased air quality index (AQI) and reduced penetration of UV B radiation. According to various studies, the consumption of exogenous vitamin D supplements and a diet rich in calcium may be beneficial for individuals residing in highly polluted areas. To address this issue, public health policies should emphasize the importance of outdoor sunlight exposure, promote a healthy diet, and reduce exposure to pollutants.

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