



## VITAMIN D LEVELS AND ADULT ASTHMA - A REVIEW

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**Abstract:** Asthma is a common life long disease affecting 300 million individuals worldwide and has a significant social and financial burden on the individuals and families affected. Factors such as genetic predisposition, allergen exposure, infections, food allergy, tobaccos smoke exposure and pollution are all proposed to influence the development and severity of asthma. Several cross-sectional studies have associated lower Vitamin D levels with decreased lung function. Focusing on the affects of vitamin D status on lung health and disease prevention this review has been written as there are limited studies highlighting the role of Vitamin D on lung function and asthma.

**Keywords:** Vitamin D, Asthma.

### INTRODUCTION

Vitamin D is an important steroid hormone having a role in bone mineralization, calcium homeostasis and wide range of conditions from cancer to fertility to longevity. Recently, research has found that Vitamin D may play an important role in multiple chronic diseases like cancer, autoimmune diseases, infections, cardiovascular disorders and one the most important the respiratory diseases.<sup>1,2</sup>

#### Sources of Vitamin D

There are two main sources of Vitamin D, one is direct skin exposure to sunlight and the other is dietary intake. Dietary sources are fish oil, fish, liver, egg yolk and dietary supplements.<sup>3</sup> As very few foods contain Vitamin D, sunlight exposure is the main primary determinant of vitamin D status in humans. In a fair skin person 20-30 minutes of sunlight exposure on the face and forearms at midday is estimated to generate an equivalent of around 2000 IU of Vitamin D. Two to three such sunlight exposures in a week are sufficient to achieve healthy vitamin D in UK.<sup>4</sup> In the absence of adequate exposure, at least 800-1000 IU (20-25ug/dl) of Vitamin D per day is needed to achieve this.<sup>2</sup>

#### Physiology of Vitamin D

Vitamin D formed from skin exposure to sunlight or obtained from dietary sources enters the circulation and is first hydroxylated at the 25 position by 25-hydroxylase to form its major circulating form, 25(OH)D, which has a circulating half life of around 3 weeks. The 25(OH)D then circulates to the kidney where it is hydroxylated at the 1-position by an 1 $\alpha$ -hydroxylase to form the hormonal form of Vitamin D which is: 1,25(OH)<sub>2</sub>D.<sup>5</sup>

Other tissues such as the epithelial lining of the lungs and immune cells also possess 1 $\alpha$ -hydroxylase activity to produce local concentration of 1,25(OH)<sub>2</sub>D which has a proposed extra-renal effects on respiratory system increasing anti microbial peptide production, regulation of the inflammatory response and airway remodeling. Vitamin D may also play an important role in respiratory muscle functioning.<sup>5</sup>

#### Vitamin D Deficiency/Insufficiency

Vitamin D insufficiency is being increasingly recognized in the general population and has been largely attributed to dietary, lifestyle and behavioral changes.<sup>6</sup> Cross sectional data indicates that there are low levels of 25(OH)D in patients with mild to moderate asthma which are correlated with poor asthma control, reduced glucocorticoid response, frequent exacerbations.<sup>7,8</sup>

25(OH)D is the best indicator of overall Vitamin D status because this measurement reflects total Vitamin D from dietary intake, sun exposure, as well as Vitamin D from adipose stores in liver. Though there are no consensus guidelines available on optimal levels of serum 25(OH)D but as defined by experts. Vitamin D deficiency is defined as a 25(OH)D levels of less than 50 nmol/l (20ng/ml)<sup>9-12</sup>. 25(OH)D levels are inversely related to parathyroid hormone levels until the former reach 75-100nmol/l (30-40ng/ml) at which point parathyroid hormone levels begin to level off.<sup>12-14</sup>

Higher Vitamin D concentration assessed by 25-hydroxy vitamin D (25(OH)D) have been associated with better lung function as measured by FEV<sub>1</sub> in a large cross-sectional study of the US population.<sup>15</sup>

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### Mechanism of Vitamin D in the Pathology of Asthma

Vitamin D deficiency is a common medical condition worldwide with more than 1 billion children and adults at risk.<sup>16</sup> The biological action of Vitamin D is far beyond calcium -phosphate homeostasis and bone metabolism. Vitamin D receptor (VDR) is also found in organs that are not typically involved in bone metabolism like immune system (such as activated T and B cells, monocytes, antigens presenting cells (APC's) including macrophages and dendritic cells.<sup>17,18</sup>

Asthma is driven by enhanced activity of Th-2 cells which induce IgE production and promote eosinophilic airway inflammation and airway hyper-responsiveness.<sup>19,20</sup> Vitamin D has a multiple cytokine modulating affects through several different cells of immune system in vitro. T cells have shown to be direct targets for 1,25(OH)<sub>2</sub>D<sup>21</sup> and a five fold increase in VDR expression has been reported after activation of quiescent CD4+ cells.<sup>17</sup>

Immune cells also have an enzymatic machinery required to activate 1, 25(OH) <sub>2</sub>D. 1, 25(OH) <sub>2</sub>D is able to traverse the cell membrane and act within the cell by binding to VDR in the nucleus. Studies suggest that dosages may also affect. For eg.1, 25(OH) <sub>2</sub>D inhibited both Th1 and Th2 cytokine production in culture of human CD4+ T cells indicating its role in asthma.

Essentially all studies using mouse or human cells agree on the capacity of Vitamin D to inhibit T cell proliferation and Th1 responses. More recently, Vitamin D has been shown to inhibit the IL-17 responses<sup>22</sup> which may be important in steroid refractory airway disease and asthma.<sup>23</sup>

Treatment with Vitamin D resulted in reduced IL-4 concentration in broncho-alveolar lavage fluid and an attenuated inflammatory response in vivo in the Th-2 dependent murine model of allergic airway disease.<sup>24</sup> It had shown to impair recruitment of eosinophils and reduced levels of interleukin-5.<sup>25</sup>

Vitamin D also enhance the production of the anti inflammatory cytokine IL-10 by human T cells in vitro and vivo both directly<sup>26</sup> and in concert with glucocorticoids.<sup>27</sup> Enhancement of IL-10 synthesis by B cells<sup>28</sup> on action of Vitamin D had also been reported.

In innate cells Vitamin D is generally believed to promote anti-microbial pathways.<sup>29</sup> and impair antigen presenting cell functioning.<sup>17,18</sup> Studies demonstrate the capacity of Vitamin D to induce the IL-10 production by dendritic cells<sup>30</sup> and a tolerogenic phenotype in these cells that promote regulatory T cells.<sup>31,32</sup>

### DISCUSSION AND CONCLUSION

The purpose of this review is to examine the current evidence for the protective role of Vitamin D in lung diseases like asthma, CF (cystic fibrosis), interstitial lung disease, COPD (chronic obstructive pulmonary disease) and respiratory infections. At this time there is a considerable amount of evidence that implicate Vitamin D as a factor associated with chronic lung disease. The question remains whether Vitamin D deficiency contributes to the etiology of lung disease or if Vitamin D deficiency is simply a manifestation of the lung disease and/or its treatment. As research in this field unfolds vitamin D supplementation is needed to be evaluated in larger trials focusing on specific respiratory disease. Therefore more research is needed to study the potential mechanism by which Vitamin D protects respiratory diseases.

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