e-ISSN: 2774-2962

Community Medicine and Education Journal

CMEJ

https://hmpublisher.com/index.php/cmej

Vitamin D Status and Lung Function in Stable COPD: A Cross-Sectional Study

Ayu Zulhafni Lubis[1*]

[1]Faculty of Medicine, Institut Kesehatan Deli Husada, Deli Tua, Indonesia

ARTICLE INFO

Keywords:
25-hydroxyvitamin D
Chronic obstructive pulmonary disease
FEV1
Lung function
Vitamin D

***Corresponding author:**
Ayu Zulhafni Lubis

E-mail address:
lubisayuzulhafni@gmail.com

The author has reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/cmej.v5i3.622

A B S T R A C T

Chronic obstructive pulmonary disease (COPD) is a major global health concern characterized by progressive airflow limitation. Vitamin D deficiency has been linked to impaired lung function and increased inflammation, suggesting a potential role in COPD pathogenesis. This study aimed to investigate the relationship between vitamin D status and lung function in patients with stable COPD. A cross-sectional study was conducted involving 51 stable COPD patients. Spirometry was performed to assess lung function, and serum 25-hydroxyvitamin D [25(OH)D] levels were measured. The association between 25(OH)D levels and lung function parameters, including forced expiratory volume in one second (FEV1), was analyzed using Pearson correlation. The mean age of the participants was 64.05 ± 8.05 years, and all were male. The majority (47.1%) had severe airflow limitation (FEV1 < 30% predicted). The mean 25(OH)D level was 27.57 ± 6.74 ng/mL, indicating insufficiency in most patients. No significant correlation was found between 25(OH)D levels and FEV1 (r = -0.131, p = 0.180). In conclusion, this study did not find a significant association between vitamin D status and lung function in stable COPD patients. Further research, including longitudinal studies and interventional trials, is needed to elucidate the complex relationship between vitamin D and COPD and to determine the potential benefits of vitamin D supplementation in this population.

1. Introduction

Chronic obstructive pulmonary disease (COPD) stands as a formidable global health challenge, characterized by persistent airflow limitation that progressively deteriorates over time. The World Health Organization (WHO) estimates that COPD was responsible for 3.23 million deaths in 2019, making it the third leading cause of mortality worldwide.[1] The burden of COPD extends beyond mortality, significantly impacting patients' quality of life and imposing a substantial economic burden on healthcare systems.[2] The primary hallmark of COPD is airflow obstruction, primarily caused by chronic inflammation, oxidative stress, and structural changes in the airways and lung parenchyma.[3] The clinical manifestations of COPD encompass a range of respiratory symptoms, including chronic cough, sputum production, dyspnea, and exercise intolerance, which collectively contribute to a diminished quality of life for affected individuals.[4] Vitamin D, traditionally recognized for its pivotal role in calcium homeostasis and bone health, has garnered increasing attention for its pleiotropic effects on various physiological processes, including immune regulation and inflammation.[5] The active form of vitamin D, 1,25-dihydroxyvitamin D, exerts its biological actions by binding to the vitamin D receptor (VDR), a nuclear transcription factor that regulates the expression of numerous genes involved in immune function, cell proliferation, and differentiation.[6] Vitamin D deficiency, defined as a serum 25-hydroxyvitamin D [25(OH)D] level below 20 ng/mL, has been linked to an elevated risk of various chronic diseases, including respiratory infections, asthma, and other respiratory conditions.[7]

The potential role of vitamin D in COPD pathogenesis has been a subject of growing interest in recent years. Several observational studies have

reported an association between low vitamin D levels and adverse outcomes in COPD patients, including impaired lung function, increased exacerbation frequency, and reduced quality of life.[8-10] The mechanisms underlying this association are multifaceted and involve the complex interplay between vitamin D, inflammation, and lung function. Chronic inflammation is a central feature of COPD pathogenesis, characterized by an imbalance between pro-inflammatory and anti-inflammatory mediators in the airways and lung parenchyma.[1] Vitamin D has been shown to modulate the immune response by suppressing pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), and enhancing the production of anti-microbial peptides, such as cathelicidin.[2] These immunomodulatory effects of vitamin D may contribute to its potential protective role in COPD by mitigating chronic inflammation and promoting immune homeostasis. Oxidative stress, arising from an imbalance between the production of reactive oxygen species (ROS) and antioxidant defenses, plays a crucial role in COPD pathogenesis.[3] ROS can damage cellular components, including DNA, proteins, and lipids, leading to inflammation, tissue remodeling, and impaired lung function.[4] Vitamin D has been shown to possess antioxidant properties, scavenging ROS and upregulating antioxidant enzymes, such as superoxide dismutase (SOD) and glutathione peroxidase (GPx).[5] These antioxidant effects of vitamin D may contribute to its potential protective role in COPD by mitigating oxidative stress and its deleterious consequences.

Lung function, as assessed by spirometry, is a key indicator of COPD severity and prognosis.[6] Forced expiratory volume in one second (FEV1), the volume of air exhaled in the first second of forced expiration, is a widely used measure of airflow limitation in COPD.[7] Several studies have reported an association between low vitamin D levels and reduced FEV1 in COPD patients, suggesting a potential role of vitamin D in preserving lung function.[8,9] The mechanisms underlying this association may involve the immunomodulatory, antioxidant, and anti-fibrotic effects of vitamin D, which could collectively contribute to the maintenance of airway and lung parenchyma integrity. Exacerbations, defined as acute worsening of respiratory symptoms beyond normal day-to-day variations, are a major cause of morbidity and mortality in COPD. Exacerbations are often triggered by respiratory infections, which can further exacerbate inflammation and airflow limitation.[1] Vitamin D deficiency has been associated with an increased risk of respiratory infections, suggesting a potential role in COPD exacerbation susceptibility.[2] Some studies have reported an association between low vitamin D levels and increased exacerbation frequency in COPD patients, although the evidence remains inconclusive.[3,4] Quality of life is an important outcome measure in COPD, reflecting the physical, emotional, and social well-being of patients.[5] COPD can significantly impair patients' quality of life due to respiratory symptoms, exercise limitation, and the psychological burden of the disease.[6] Vitamin D deficiency has been associated with reduced quality of life in various chronic diseases, including COPD.[7] The mechanisms underlying this association may involve the effects of vitamin D on muscle function, inflammation, and psychological well-being. Despite the growing body of evidence linking vitamin D to COPD, there are still gaps in our understanding of this complex relationship. The inconsistency in the findings of previous studies highlights the need for further research to elucidate the role of vitamin D in COPD pathogenesis and to determine the potential benefits of vitamin D supplementation in this population. This study aimed to investigate the relationship between vitamin D status and lung function in patients with stable COPD. We hypothesized that lower vitamin D levels would be associated with poorer lung function, as measured by FEV1. We also explored the potential confounding effects of age, smoking history, and comorbidities on this association.

2. Methods

This investigation employed a cross-sectional study design, aiming to capture a snapshot of the relationship between vitamin D status and lung function in patients with stable COPD. The study was conducted at the lung disease polyclinic of a tertiary care hospital in North Sumatera, Indonesia. This setting was chosen due to its high volume of COPD patients, allowing for the recruitment of a representative sample. The cross-sectional nature of the study enables the efficient collection of data at a single point in time, making it feasible within the constraints of resources and time. However, it is important to acknowledge that this design limits the ability to establish causality, as it only provides a snapshot of the association between variables at a particular moment. The study population consisted of male patients diagnosed with stable COPD, defined as the absence of exacerbations in the four weeks preceding enrollment. The focus on male patients was driven by the observation that COPD prevalence is higher in men than in women, and the potential influence of gender on vitamin D metabolism and its impact on lung function. The age criterion of over 40 years was set to ensure that the participants had a sufficient duration of exposure to risk factors for COPD, such as smoking and environmental pollutants. The willingness to participate and provide informed consent was essential to ensure ethical conduct and protect the autonomy of the participants. The exclusion criteria were carefully defined to minimize confounding factors and ensure the homogeneity of the study population. Patients with acute exacerbations of COPD were excluded to avoid the acute inflammatory response influencing lung function and vitamin D levels. The exclusion of patients with asthma was aimed at preventing the overlap of airway obstruction patterns between the two conditions. Abnormal leukocyte counts were excluded to rule out the presence of active infections or other inflammatory conditions that could affect both lung function and vitamin D status. Finally, patients taking medications known to influence hs-CRP levels or vitamin D metabolism were excluded to prevent these medications from confounding the relationship between vitamin D and lung function.

The sample size of 51 patients was determined based on a power analysis, considering the expected effect size, desired level of statistical significance, and power. The purposive sampling technique was employed to select participants who met the inclusion and exclusion criteria. This non-probability sampling method allows for the selection of participants based on specific characteristics relevant to the research question. While purposive sampling may introduce some selection bias, it is often used in clinical research when the target population is relatively small or difficult to access. Data collection involved a combination of interviews, medical record reviews, and laboratory assessments. Demographic information, such as age, occupation, and smoking history, was collected through structured interviews. Medical records were reviewed to confirm the diagnosis of COPD, assess disease severity, and identify any comorbidities. Lung function was evaluated using spirometry, a standard pulmonary function test that measures the volume and flow of air during forced expiration. The forced expiratory volume in one second (FEV1) was recorded as the primary outcome measure, expressed as a percentage of the predicted value based on age, height, and gender. Serum 25-hydroxyvitamin D [25(OH)D] levels were measured using the Vidas Biomerieux assay, a commercially available immunoassay that quantifies the concentration of 25(OH)D in serum or plasma. This assay is widely used in clinical practice and research due to its high sensitivity and specificity. Vitamin D status was categorized based on established cutoffs: deficiency (<20 ng/mL), insufficiency (20-29.9 ng/mL), sufficiency (30-100 ng/mL), and toxicity (>100 ng/mL).

The collected data were analyzed using SPSS software, a comprehensive statistical package widely used in medical research. Descriptive statistics, including means, standard deviations, frequencies, and percentages, were used to summarize the

characteristics of the study population and the distribution of key variables. Pearson correlation analysis was employed to assess the association between 25(OH)D levels and FEV1. This statistical test measures the strength and direction of the linear relationship between two continuous variables. A p-value less than 0.05 was considered statistically significant, indicating a low probability that the observed association occurred by chance. The study protocol was approved by the Institutional Review Board of the hospital North Sumatera, Indonesia, ensuring that it adhered to ethical principles and guidelines for research involving human subjects. All participants provided written informed consent after receiving a detailed explanation of the study's purpose, procedures, potential risks and benefits, and their right to withdraw at any time without consequences. Confidentiality was maintained throughout the study, and data were anonymized to protect the privacy of the participants.

3. Results and Discussion

Table 1 summarizes the key demographic, clinical, and laboratory findings of the 51 male COPD patients included in the study. The average age of participants was 64, with most being retired, reflecting the typical demographic of COPD patients. The mean FEV1 of 33.65% predicted indicates severe airflow limitation, highlighting the significant impact of COPD on lung function within this group. The presence of comorbidities like hypertension, diabetes, and cardiovascular disease underscores the multi-faceted health challenges often faced by COPD patients. These conditions can interact with COPD, potentially influencing disease progression and management. The mean 25(OH)D level of 27.57 ng/mL falls within the insufficient range, with a significant proportion (45.1%) of participants exhibiting insufficiency and 15.7% having outright deficiency. This observation emphasizes the high prevalence of vitamin D inadequacy in this COPD cohort, raising questions about its potential implications for disease management and outcomes. Overall, Table 1 paints a picture of a group of elderly male COPD patients with severe airflow limitation and a high prevalence of vitamin D insufficiency. These findings set the stage for exploring the relationship between vitamin D status and lung function in this population, as investigated in the subsequent sections of the study.

Table 1. Participant characteristics.

Characteristic	Value
Number of participants (n)	51
Mean age (years)	64.05 ± 8.05
Gender	All male
Employment status	
Retired	54.9%
Other	45.1%
Comorbidities	
Hypertension	31.4%
Diabetes mellitus	19.6%
Cardiovascular disease	15.7%
Other	33.3%
Mean FEV1 (% predicted)	33.65 ± 15.78
Mean 25(OH)D level (ng/mL)	27.57 ± 6.74
Vitamin D status	
Insufficient (20-29.9 ng/mL)	45.1%
Deficient (<20 ng/mL)	15.7%
Sufficient (30-100 ng/mL)	39.2%

Table 2 and Figure 1 illustrate the statistical analysis examining the relationship between 25(OH) vitamin D levels and FEV1 (a measure of lung function) in the study population. The Pearson correlation coefficient (r) of -0.131 suggests a weak, negative correlation between 25(OH)D levels and FEV1. This implies that, in general, as 25(OH)D levels increase, FEV1 tends to slightly decrease, although this trend is very subtle. The p-value of 0.180, however, indicates that this correlation is not statistically significant. In other words, the observed trend could likely have occurred by chance, and there is not enough evidence to conclude that a true relationship exists between these two variables in the population. The scatter plot visually depicts the relationship between 25(OH)D levels and FEV1 for each individual in the study. The lack of a clear pattern or trend in the distribution of the points aligns with the non-significant correlation found in Table 2. If there were a strong correlation, we would expect to see the points clustered more closely around a line, either sloping upwards (for a positive correlation) or downwards (for a negative correlation). The scattered nature of the points in this plot further emphasizes the absence of a strong association between the two variables. The data presented in Table 2 and Figure 1 suggest that there is no statistically significant relationship between vitamin D status and lung function (as measured by FEV1) in this group of stable COPD patients.

Table 2. Correlation test of FEV1 with 25(OH) vitamin D levels.

Variable	**25(OH) vitamin D**
FEV1	
r	-0.131*
p	0.180**

*Pearson test; **Significant p-value <0.05.

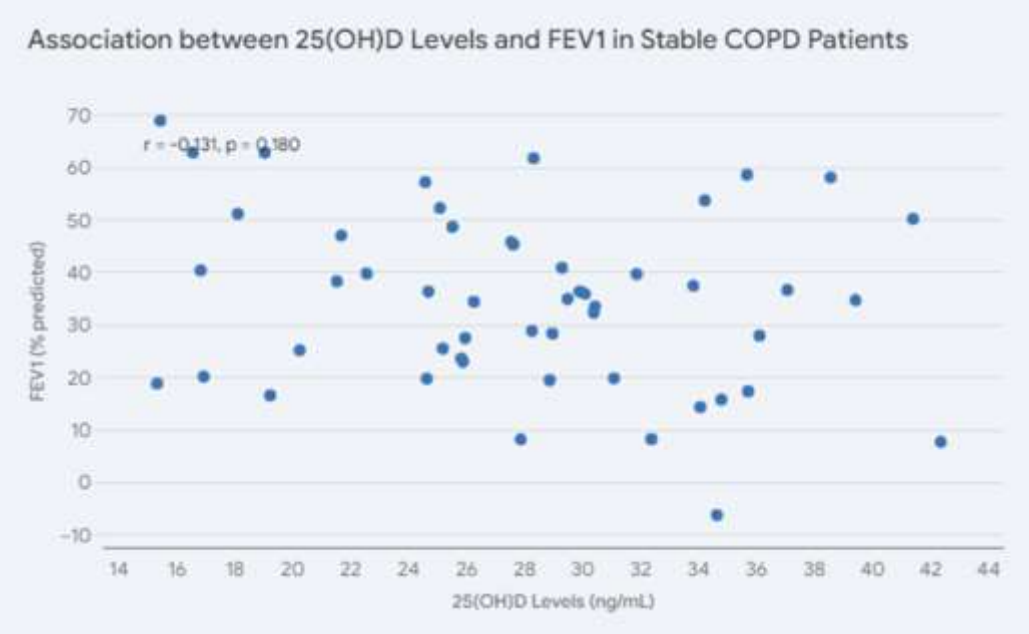

Figure 1. Association between 25(OH)D levels and FEV1 in stable COPD patients.

The role of body composition in influencing vitamin D levels, particularly the contrast between men and women, is a multifaceted and intriguing area of research. The observation that women tend to have higher serum 25(OH)D levels than men, even when factors like sun exposure and dietary intake are controlled, suggests that inherent physiological differences play a significant role. The distinct body composition of women, characterized by a higher percentage of body fat, emerges as a key player in this dynamic. Vitamin D, classified as a fat-soluble vitamin, possesses an inherent affinity for adipose tissue, or body fat. This lipophilic nature allows vitamin D to readily dissolve and accumulate within fat cells, effectively creating a reservoir for this essential nutrient. Consequently, the greater fat reserves typically found in women, compared to men, can serve as a more expansive storage space for vitamin D. This enhanced storage capacity may contribute to the elevated serum 25(OH)D levels observed in women, even in scenarios where their vitamin D intake or synthesis is not significantly higher than that of men. The fat tissue acts as a buffer, sequestering vitamin D and gradually releasing it into circulation, thereby maintaining a more stable serum concentration. The implications of this fat reservoir are particularly relevant in the context of vitamin D deficiency. In situations where dietary intake or sun exposure is limited, individuals with higher body fat percentages may be able to draw upon their vitamin D stores for a longer duration, potentially delaying the onset of deficiency symptoms. Conversely, individuals with lower body fat percentages may be more susceptible to rapid depletion of vitamin D stores and the associated health consequences.[9-11]

The influence of body composition on vitamin D dynamics extends beyond the mere quantity of fat. The distribution of fat also plays a crucial role. Women tend to have a greater proportion of subcutaneous fat, which is located just beneath the skin, while men tend to have more visceral fat, which surrounds internal organs. This distinction in fat distribution may have implications for vitamin D bioavailability and metabolism. Subcutaneous fat, being more readily accessible, may facilitate the storage and release of vitamin D. The proximity of subcutaneous fat to the skin may also enhance the cutaneous synthesis of vitamin D, as sunlight exposure is a key trigger for this process. In contrast, visceral fat, being deeper within the body, may be less accessible for vitamin D storage and release. Moreover, visceral fat has been associated with metabolic dysfunction and inflammation, which could potentially interfere with vitamin D metabolism and its physiological effects. The impact of these gender-specific differences in fat distribution on vitamin D dynamics is an area that warrants further investigation. Understanding how subcutaneous and visceral fat differentially influence vitamin D storage, release, and metabolism could provide valuable insights into the complex relationship between body composition and vitamin D status.[10-12]

While the concept of fat tissue serving as a reservoir for vitamin D is well-established, the precise mechanisms governing the storage, release, and mobilization of vitamin D from adipose tissue remain an area of active research. The size and metabolic activity of adipocytes, the cells that constitute fat tissue, may affect their capacity to store and release vitamin D. Larger adipocytes may have a greater storage capacity, while smaller, more metabolically active adipocytes may be more efficient in releasing vitamin D into circulation. Adipose tissue secretes a variety of signaling molecules called adipokines, which can influence various physiological processes, including inflammation, insulin sensitivity, and energy metabolism. Certain adipokines may also interact with vitamin D metabolism, potentially modulating its bioavailability and effects. Chronic inflammation, often associated with obesity and metabolic dysfunction, may interfere with vitamin D metabolism and signaling. Inflammatory cytokines can downregulate vitamin D receptor expression and activity, potentially impairing the body's response to vitamin D. Other factors, such as age, genetics, and lifestyle habits, may also influence the relationship between body composition and vitamin D dynamics.

Further research is needed to fully elucidate these complex interactions. The distinct body composition of women, characterized by a higher percentage of body fat and a greater proportion of subcutaneous fat, plays a pivotal role in vitamin D dynamics. The fat tissue acts as a reservoir for vitamin D, contributing to higher serum levels observed in women compared to men. The distribution of fat, with its implications for vitamin D storage, release, and metabolism, further underscores the importance of body composition in understanding gender differences in vitamin D status.The human genome harbors a vast array of genetic variations that can influence various aspects of physiology, including vitamin D metabolism. Certain genetic polymorphisms have been associated with alterations in vitamin D receptor expression and activity. The vitamin D receptor is a nuclear hormone receptor that mediates the biological effects of vitamin D by regulating gene transcription. Variations in receptor expression or activity can affect the body's responsiveness to vitamin D, potentially leading to differences in serum levels and physiological outcomes. Gender-specific genetic variations may exist that contribute to the observed disparities in vitamin D metabolism between men and women. These variations could influence the efficiency of vitamin D absorption, transport, storage, or activation, ultimately impacting serum levels. Unraveling the complex interplay between genetic factors and gender in vitamin D metabolism is an area of active research that holds promise for personalized approaches to vitamin D supplementation and disease prevention.[11-13]

While body composition, hormonal influences, and genetic factors are likely key contributors to gender differences in vitamin D metabolism, other factors may also play a role. Differences in sun exposure habits between men and women may contribute to variations in vitamin D levels. However, studies that have controlled for sun exposure have still observed gender disparities in vitamin D status, suggesting that other factors are also at play. Dietary intake of vitamin D can vary between genders, potentially influencing serum levels. However, the contribution of dietary intake to the observed gender differences is likely to be modest, as most individuals do not obtain sufficient vitamin D from diet alone. Certain medications, such as anticonvulsants and glucocorticoids, can interfere with vitamin D metabolism and lower serum levels. Gender differences in medication use may contribute to variations in vitamin D status.[12-14]

The hormonal milieu, particularly the presence of estrogen, the primary female sex hormone, exerts a profound influence on the intricate pathways of vitamin D metabolism. The dynamic interplay between estrogen and vitamin D metabolism has far-reaching implications for various physiological processes, including calcium homeostasis, bone health, and immune function. The potential of estrogen to modulate the activity of 1α-hydroxylase, the key enzyme responsible for the conversion of 25(OH)D to its active form, 1,25-dihydroxyvitamin D [1,25(OH)2D], has garnered significant attention in recent years. The conversion of 25(OH)D, the major circulating form of vitamin D, to its active form, 1,25(OH)2D, is a tightly regulated process that occurs primarily in the kidneys. The enzyme 1α-hydroxylase catalyzes this crucial step, and its activity is subject to modulation by various factors, including parathyroid hormone, calcium levels, and, notably, estrogen. The active form of vitamin D, 1,25(OH)2D, binds to the vitamin D receptor (VDR), a nuclear hormone receptor that regulates gene transcription. The VDR is expressed in a wide range of tissues, including the intestines, kidneys, bone, and immune cells, highlighting the pleiotropic effects of vitamin D. Estrogen, through its interaction with estrogen receptors, has been shown to influence the expression and activity of 1α-hydroxylase. Studies have demonstrated that estrogen can upregulate 1α-hydroxylase gene expression, leading to increased enzyme activity and subsequent production of 1,25(OH)2D. This estrogen-mediated upregulation of 1α-hydroxylase may contribute to the higher serum 25(OH)D levels observed in women compared to men. The mechanism by which estrogen influences 1α-

hydroxylase activity is complex and involves multiple signaling pathways. Estrogen receptors can directly bind to regulatory elements in the 1α-hydroxylase gene, promoting its transcription. Additionally, estrogen may indirectly influence 1α-hydroxylase activity through its effects on other hormones and signaling molecules, such as parathyroid hormone and fibroblast growth factor-23 (FGF-23).[12-14]

The body strives to maintain a delicate balance between the storage form of vitamin D (25(OH)D) and its active form (1,25(OH)2D). The increased production of 1,25(OH)2D in women, potentially driven by estrogen-mediated upregulation of 1α-hydroxylase, may lead to a compensatory increase in 25(OH)D levels. This compensatory mechanism aims to ensure an adequate supply of the storage form to meet the demands for active vitamin D synthesis. The intricate relationship between estrogen and vitamin D metabolism highlights the importance of considering hormonal influences when interpreting gender differences in vitamin D status. The fluctuations in estrogen levels throughout a woman's life, such as during puberty, pregnancy, and menopause, may have significant implications for vitamin D metabolism and its associated health outcomes. The influence of estrogen on vitamin D metabolism extends beyond its impact on serum 25(OH)D levels. It may also affect the tissue-specific actions of vitamin D, as the expression and activity of the VDR can be modulated by estrogen. This complex interplay between estrogen and vitamin D signaling pathways may have implications for various physiological processes, including bone health, immune function, and cardiovascular health. Understanding the intricate relationship between estrogen and vitamin D metabolism is crucial for optimizing vitamin D status and preventing vitamin D-related health problems in women. Further research is needed to elucidate the precise mechanisms by which estrogen influences vitamin D metabolism and to determine the clinical implications of these gender-specific differences. This knowledge may lead to the development of tailored approaches to vitamin D supplementation and disease prevention strategies that consider the unique hormonal milieu of women.[13-15]

The human genome, the blueprint of life, is a tapestry woven with an intricate array of genetic variations that contribute to the rich diversity observed among individuals. These variations, often referred to as polymorphisms, can influence various aspects of human physiology, including the metabolism of vital nutrients such as vitamin D. The complex interplay between genetic factors and gender in vitamin D metabolism is an area of active research, holding the promise of personalized approaches to supplementation and disease prevention. At the heart of vitamin D's biological effects lies the vitamin D receptor (VDR), a nuclear hormone receptor that acts as a molecular switch, turning genes on or off in response to the presence of the active form of vitamin D, 1,25-dihydroxyvitamin D [1,25(OH)2D]. The VDR is expressed in a wide range of tissues, including the intestines, kidneys, bone, and immune cells, reflecting the pleiotropic actions of vitamin D. Upon binding to 1,25(OH)2D, the VDR forms a complex with another nuclear receptor, the retinoid X receptor (RXR). This complex then binds to specific DNA sequences, known as vitamin D response elements (VDREs), located in the regulatory regions of target genes. The binding of the VDR-RXR complex to VDREs can either enhance or suppress gene transcription, leading to changes in protein synthesis and cellular function. The VDR plays a critical role in mediating the diverse biological effects of vitamin D, including calcium absorption, bone mineralization, immune regulation, and cell growth and differentiation. The activity of the VDR is tightly regulated at multiple levels, including gene expression, protein stability, and ligand binding affinity. Genetic variations that affect any of these regulatory mechanisms can influence the body's responsiveness to vitamin D, potentially leading to differences in serum levels and physiological outcomes.[14-16]

The human genome is peppered with millions of single nucleotide polymorphisms (SNPs), which are variations in a single DNA building block. These SNPs can occur in coding or non-coding regions of the

genome and can have varying effects on gene function. Several SNPs have been identified in the VDR gene that are associated with alterations in VDR expression or activity. One of the most extensively studied VDR polymorphisms is the TaqI polymorphism, located in exon 9 of the VDR gene. This polymorphism results in a change from a T to a C nucleotide, leading to a synonymous change in the amino acid sequence of the VDR protein. However, this seemingly silent change has been associated with differences in VDR mRNA stability and protein expression, potentially influencing the body's response to vitamin D. Another well-characterized VDR polymorphism is the BsmI polymorphism, located in intron 8 of the VDR gene. This polymorphism results in a change from a B to a b allele, which has been associated with differences in VDR gene transcription and protein levels. The FokI polymorphism, located in exon 2 of the VDR gene, results in a change from an F to an f allele. This change leads to the production of a VDR protein that is three amino acids shorter than the full-length protein. The shorter VDR protein has been shown to have increased transcriptional activity, potentially influencing the expression of vitamin D target genes. Several other VDR polymorphisms have been identified, including ApaI, Cdx2, and poly(A) polymorphisms. These polymorphisms have been associated with variations in VDR expression, activity, and ligand binding affinity, potentially influencing the body's response to vitamin D.[15-17]

While the aforementioned VDR polymorphisms are present in both men and women, there is emerging evidence suggesting that gender-specific genetic variations may also exist that contribute to the observed disparities in vitamin D metabolism between the sexes. Genetic variations in genes involved in intestinal vitamin D absorption, such as the cubilin gene and the megalin gene, could lead to differences in the efficiency of vitamin D uptake from the diet. Genetic variations in genes encoding vitamin D binding protein (DBP), the main carrier of vitamin D in the blood, could affect the transport of vitamin D to target tissues. Genetic variations in genes involved in vitamin D storage in adipose tissue, such as the lipoprotein lipase gene and the fatty acid binding protein 4 gene, could influence the capacity for vitamin D storage and release. Genetic variations in genes encoding enzymes involved in vitamin D activation, such as the CYP2R1 gene and the CYP27B1 gene, could affect the conversion of vitamin D to its active form.[18-20]

4. Conclusion

This cross-sectional study did not find a significant association between vitamin D status and lung function in stable COPD patients. However, further research is needed to fully elucidate the complex relationship between vitamin D and COPD. Longitudinal studies and interventional trials are warranted to determine whether vitamin D supplementation can improve lung function, reduce exacerbation frequency, and enhance the quality of life in COPD patients.

5. References

1. Brandsma CA, Van den Berge M, Hackett TL, Brusselle G, Timens W. Recent advances in chronic obstructive pulmonary disease pathogenesis: from disease mechanisms to precision medicine. J Pathol. 2020; 250(5): 624–35.
2. AL Wachami N, Guennouni M, Iderdar Y, Boumendil K, Arraji M, Mourajid Y, et al. Estimating the global prevalence of chronic obstructive pulmonary disease (COPD): a systematic review and meta-analysis. BMC Public Health. 2024; 24(1): 1–16.
3. Tanumihardja JP, Nurwahyuni A. The impact of chronic obstructive lung clinical pathway implementation on readmission: a systematic review. 2019; 338–8.
4. Ciocarlie T, Motofelea AC, Motofelea N, Dutu AG, Crăciun A, Costachescu D, et al. Exploring the role of vitamin D, vitamin D-dependent proteins, and vitamin D receptor gene variation in lung cancer risk. Int J Mol Sci. 2024;25(12).

5. Fernandez-Robredo P, González-Zamora J, Recalde S, Bilbao-Malavé V, Bezunartea J, Hernandez M, et al. Vitamin D protects against oxidative stress and inflammation in human retinal cells. Antioxidants. 2020; 9(9): 1–18.
6. Lokesh KS, Chaya SK, Jayaraj BS, Praveena AS, Krishna M, Madhivanan P, et al. Vitamin D deficiency is associated with chronic obstructive pulmonary disease and exacerbation of COPD. Clin Respir J. 2021; 15(4): 389–99.
7. Sharifi H, Ghanei M, Jamaati H, Masjedi MR, Najafimehr H, Fakharian A, et al. Effect of COPD on health-related quality of life; results from the BOLD study in Iran. Tanaffos. 2021; 20(1): 51–8.
8. Lu Z, Coll P, Maitre B, Epaud R, Lanone S. Air pollution as an early determinant of COPD. Eur Respir Rev. 2022; 31(165): 1–13.
9. Baarnes CB, Thuesen BH, Linneberg A, Ustrup AS, Pedersen SK, Ulrik CS. Predictors of accelerated FEV1 decline in adults with airflow limitation—Findings from the Health2006 cohort. Chron Respir Dis. 2019; 16.
10. Casado E, Costa E, Mezquita-Raya P, Andújar-Espinosa R, Neyro JL. Calcifediol in the management of vitamin D deficiency-related skeletal and extraskeletal diseases: overview and clinical cases. Drugs Context. 2023; 12.
11. Zhu Z, Wan X, Liu J, Zhang D, Luo P, Du W, et al. Vitamin D status and chronic obstructive pulmonary disease risk: a prospective UK Biobank study. BMJ Open Respir Res. 2023; 10(1): 1–8.
12. Li M. The role of vitamin D in chronic obstructive pulmonary disease with pulmonary hypertension. Pulm Circ. 2023; 13(4): 1–10.
13. Li Y, Gao H, Zhao L, Wang J. Osteoporosis in COPD patients: Risk factors and pulmonary rehabilitation. Clin Respir J. 2022; 16(7): 487–96.
14. Baek MS, Yoon DS, Park JS, Yoon BW, Oh BS, Park J, et al. Vitamin D inhibits expression and activity of matrix metalloproteinase in human lung fibroblasts (HFL-1) cells. Tuberc Respir Dis (Seoul). 2014; 77(2): 73–80.
15. Octavius GS, Daleni VA, Angeline G, Virliani C. A systematic review and meta-analysis of prevalence of vitamin D deficiency among Indonesian pregnant women: a public health emergency. AJOG Glob Reports. 2023; 3(2): 10–9.
16. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2023 report.
17. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med. 2007; 176(6): 532-55.
18. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. Lancet. 2006; 367(9524): 1747-57.
19. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med. 2006; 3(11): e442.
20. WHO. Global Health Estimates 2016: deaths by cause, age, sex, by country and by region, 2000-2016. Geneva: World Health Organization; 2018.