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Exploring the Role of Vitamin D3 in Addressing Lung Dysfunction and Small Airways Degeneration in Chronic Obstructive Pulmonary Disease

Hina Benish Khan¹, Munila Shabnum Khattak², Mehwish Durrani³, Atif Hussain⁴, Sara Yar Khan⁵, Aziz Ur Rehman⁶✉

¹Department of Physiology, Khyber Medical College, Peshawar - Pakistan

²Department of Anatomy, Khyber Medical College, Peshawar - Pakistan

³Department of Biochemistry, Rehman Medical College, Peshawar - Pakistan

⁴Department of Anatomy, Women Medical College, Abbottabad - Pakistan

⁵Department of Biochemistry, Jinnah Medical College, Peshawar - Pakistan

⁶Department of Biochemistry, Northwest School of Medicine, Peshawar - Pakistan

Corresponding author:

Aziz Ur Rehman

Department of Biochemistry,
Northwest School of Medicine,
Peshawar - Pakistan
Email: drazizmehsud@gmail.com

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A B S T R A C T

Background: Chronic Obstructive Pulmonary Disease (COPD) presents a significant global health challenge, necessitating comprehensive investigations into potential contributors and therapeutic avenues.

Objectives: To investigate the intricate connections between dysfunctional lung anatomy, small airways degeneration, and the therapeutic potential of Vitamin D3 in COPD.

Methodology: This prospective cross-sectional study was carried out at the Hayatabad Medical Complex in Peshawar, Pakistan, in the department of pulmonology. spanning January 2020 to February 2021. A total of 189 COPD participants aged 40 to 75 were enrolled in this study. Comprehensive data collection involved clinical observations, molecular analyses, and participant interviews.

Statistical analyses, including regression, correlation assessments, and subgroup analyses, were conducted to explore the specified relationships.

Results: Significant negative associations were found between dysfunctional lung anatomy, small airways degeneration, and Vitamin D3 levels. For dysfunctional lung anatomy, the beta coefficient (β) was -0.23 ($p < 0.05$), and for small airways degeneration, it was -0.18 ($p < 0.05$). Subgroup analyses highlighted lower Vitamin D3 levels in severe COPD (25.8 ng/mL, SD = 7.5) compared to moderate cases (30.5 ng/mL, SD = 8.2).

Conclusion: The study underscores the complexity of pulmonary factors and Vitamin D3 in COPD, offering potential avenues for targeted interventions and therapeutic considerations.

Keywords: Chronic Obstructive Pulmonary Disease; Vitamin D3; Dysfunctional Lung Anatomy; Small Airways Degeneration; COPD Severity

Introduction

The complicated respiratory condition known as chronic obstructive pulmonary disease (COPD) is characterized by a gradual restriction in airflow.¹ One of the pivotal aspects contributing to COPD pathology is dysfunctional lung anatomy.² Numerous anatomical changes to the respiratory system, affecting both the big and small airways, are involved in this dysfunction. The complex interactions between these anatomical alterations have a substantial impact on respiratory health overall and worsen COPD symptoms.³ Developing focused therapies that might treat the underlying causes of this crippling illness requires a thorough understanding of the subtleties of defective lung structure.⁴

The deterioration of the small airways becomes an important part of the complex web of COPD etiology.⁵ Little airways, which are often disregarded, are essential for controlling airflow and maintaining ideal lung function.⁶ These fragile structures gradually deteriorate in people with COPD, which increases airway resistance and impairs breathing. Research in this crucial field is necessary since the complex processes behind small airways degeneration are still not completely understood.⁷ In order to develop therapies that might stop or reverse the degenerative processes and open up new paths for managing COPD, a thorough investigation of these microscopic alterations is needed.⁸

Vitamin D3's function has received a lot of interest lately in respiratory studies, especially in relation to COPD.⁹ One fat-soluble vitamin that has several physiological uses is vitamin D3, which has been linked to immune response modulation and lung health maintenance.¹⁰ Based on preliminary data, vitamin D3 may be able to help slow down the advancement of COPD by modulating immunological responses, inflammation, and possibly lung tissue repair. But further research is still needed to determine the exact mechanisms and scope of Vitamin D3's effects on COPD patients' defective lung structure and small airway deterioration.¹¹

A thorough knowledge of the interaction between defective lung structure, small airway degeneration, and the therapeutic potential of vitamin D3 is limited, despite the fact that previous research has provided light on certain aspects of COPD pathogenesis.¹²

Objective

To investigate the intricate connections between dysfunctional lung anatomy, small airways degeneration, and the therapeutic potential of Vitamin D3 in COPD.

Methodology

This prospective cross-sectional study was carried out at

the Hayatabad Medical Complex in Peshawar, Pakistan, in the department of pulmonology. spanning January 2020 to February 2021, a 12-month period.

Participants in this research include both genders with a diagnosis of COPD between the ages of 40 and 75 who provided written informed permission. Participants must reflect a range of COPD severity levels, from moderate to severe, and have confirmed vitamin D3 levels within the last six months. People having a history of respiratory conditions other than COPD, those who have had lung surgery or a transplant, and women who are pregnant or nursing are not eligible to participate in this research. In addition, individuals who were unable to provide written informed permission, had extensive sun exposure, were getting high-dose vitamin D supplements, or had chronic conditions that affected their metabolism of vitamin D were not included.

Our study commenced with an enrollment of 282 patients. However, a meticulous screening process, guided by stringent inclusion and exclusion criteria, resulted in the exclusion of 93 participants. These exclusions included 8 individuals with a history of respiratory diseases other than COPD, 14 with prior lung surgery or transplantation, 12 due to pregnancy or lactation, 15 with chronic diseases affecting Vitamin D metabolism, 9 receiving high-dose Vitamin D supplementation, 17 with significant sun exposure, 18 patients unwilling to provide written informed consent were excluded. Through this discerning selection process, we achieved a precisely tailored cohort of 189 participants. The strategic determination of this sample size, guided by thorough statistical power calculations, ensures our study's robustness in detecting meaningful associations between dysfunctional lung anatomy, small airways degeneration, and Vitamin D3 levels in COPD, significantly enhancing the reliability of our research outcomes.

Comprehensive data collection involved a multi-faceted approach encompassing clinical observations, molecular analyses, and participant interviews. The scrutiny of medical records, diagnostic tests, and imaging studies facilitated the gathering of relevant clinical information. Blood samples were collected for molecular assessments, including Vitamin D3 levels, while a structured questionnaire systematically collected sociodemographic data, lifestyle factors, and pertinent clinical details, including COPD severity and treatment history.

Descriptive statistics, including means, standard deviations, and frequencies, were utilized to summarize and characterize the demographic and clinical profiles of the study participants. Regression analyses were performed to explore the associations between dysfunctional lung anatomy, small airways degeneration, and Vitamin D3 levels, accounting for potential confounding variables. To assess the strength and direction of relationships, Pearson correlation coefficients were conducted between variables of interest. Correlations were explored between Vitamin D3 levels and markers of dysfunctional lung

Table 1. Participants Demographic and Clinical Characteristics

Characteristic	Total (n=189)	Moderate COPD (n=72)	Severe COPD (n=117)
Age (years), Mean (SD)	62.4 (7.2)	61.8 (6.5)	63.2 (7.6)
Gender, n (%)			
Male	123 (65%)	47 (65%)	76 (65%)
Female	66 (35%)	25 (35%)	41 (35%)

anatomy and small airways degeneration. Subgroup analyses were carried out to investigate potential variations in the observed relationships based on COPD severity levels. Multivariate analyses multiple regression models were applied to investigate the combined impact of dysfunctional lung anatomy and small airways degeneration on Vitamin D3 therapeutic potential while adjusting for relevant covariates. All statistical tests were two-tailed, and a significance level of 0.05 was chosen to determine statistical significance. The statistical software SPSS (version 23.0) was employed for all analyses.

To uphold ethical standards, the study obtained approval from the Institutional Review Board (IRB) at Hayatabad Medical Complex before initiation. Informed consent, emphasizing confidentiality and voluntary participation, was obtained from all participants, ensuring the ethical conduct of the research in accordance with the principles outlined in the Declaration of Helsinki.

Results

The study enrolled 189 participants with COPD, aged between 40 and 75, exhibiting a predominantly male composition, constituting 65% of the total cohort. The mean age of the participants was 62.4 years, with a standard deviation of 7.2. The cohort was diverse in COPD severity, with 38% classified as having moderate COPD and 62% with severe COPD. Subgroup analysis revealed that within the moderate COPD group (n=72), the

mean age was 61.8 years (SD = 6.5), and males comprised 65%, while females constituted 35%. In the severe COPD group (n=117), the mean age was slightly higher at 63.2 years (SD = 7.6), with 65% being male and 35% female (Table 1).

A significant associations and correlations between dysfunctional lung anatomy, small airways degeneration, and the therapeutic potential of Vitamin D3 in COPD. Dysfunctional lung anatomy exhibited a negative association with Vitamin D3 levels, with a beta coefficient (β) of -0.23 ($p < 0.05$). Similarly, small airways degeneration demonstrated a negative correlation with Vitamin D3 levels, with a beta coefficient of -0.18 ($p < 0.05$). Notably, the correlations between Vitamin D3 levels and both dysfunctional lung anatomy ($r = -0.36$, $p < 0.01$) and small airways degeneration ($r = -0.28$, $p < 0.01$) were negative and statistically significant. These findings underscore the intricate connections between pulmonary factors and Vitamin D3 levels in COPD, providing valuable insights into potential therapeutic implications (Table 2).

Significant differences in Vitamin D3 levels based on COPD severity was also found in this study. In the moderate COPD subgroup, the mean Vitamin D3 level was 30.5 ng/mL (SD = 8.2), while in the severe COPD subgroup, the mean was 25.8 ng/mL (SD = 7.5). The observed difference was statistically significant ($p < 0.01$), indicating that individuals with severe COPD had significantly lower Vitamin D3 levels compared to those with moderate COPD. This subgroup analysis unders-

Table 2. Associations and Correlations of dysfunctional lung anatomy, small airways degeneration, and the therapeutic potential of Vitamin D3 in COPD

Variable	Beta (β) / Correlation (r)	p-value
Dysfunctional Lung Anatomy	-0.23	<0.05
Small Airways Degeneration	-0.18	<0.05
Vitamin D3 Levels vs. Anatomy	-0.36	<0.01
Vitamin D3 Levels vs. Airways	-0.28	<0.01

Table 3. Subgroup Analyses - Vitamin D3 Levels based on COPD Severity

COPD Severity	Vitamin D3 Levels (Mean ± SD)	p-value
Moderate COPD	30.5 ± 8.2	<0.01
Severe COPD	25.8 ± 7.5	

cores the impact of COPD severity on Vitamin D3 levels, emphasizing the potential relevance of Vitamin D3 in the context of disease severity and suggesting avenues for targeted interventions or therapeutic considerations (Table 3).

Discussion

Chronic Obstructive Pulmonary Disease (COPD) presents a significant global health challenge, necessitating comprehensive investigations into potential contributors and therapeutic avenues. The study enrolled 189 participants with COPD, aged between 40 and 75, exhibiting a predominantly male composition, constituting 65% of the total cohort. The mean age of the participants was 62.4 years, with a standard deviation of 7.2. The demographic characteristics of the study cohort, particularly the male predominance and the distribution of age and COPD severity, align with several studies on COPD. Numerous investigations have reported a higher prevalence of COPD in males, often attributing it to historical differences in smoking patterns and occupational exposures.^{13,14} The mean age of our participants (62.4 years) is consistent with the typical age range reported in COPD studies, highlighting the condition's association with aging.¹⁵ This cohort was diverse in COPD severity, with 38% classified as having moderate COPD and 62% with severe COPD. The distribution of COPD severity, with a majority classified as having severe COPD, mirrors the well-documented progressive nature of the disease.¹⁶ Subgroup analysis revealed that within the moderate COPD group (n=72), the mean age was 61.8 years (SD = 6.5), and males comprised 65%, while females constituted 35%. In the severe COPD group (n=117), the mean age was slightly higher at 63.2 years (SD = 7.6), with 65% being male and 35% female. Subgroup analyses within moderate and severe COPD groups align with studies emphasizing the need for differentiated approaches in understanding the disease's heterogeneity, considering factors such as age and gender.¹³⁻¹⁶ Our findings, therefore, reinforce and contribute to the previous findings, emphasizing the importance of comprehensively characterizing study cohorts in COPD research to better inform tailored interventions and management strategies.

In our study, Dysfunctional lung anatomy exhibited a negative association with Vitamin D3 levels, with a beta

coefficient (β) of -0.23 ($p < 0.05$). Similarly, small airways degeneration demonstrated a negative correlation with Vitamin D3 levels, with a beta coefficient of -0.18 ($p < 0.05$). Notably, the correlations between Vitamin D3 levels and both dysfunctional lung anatomy ($r = -0.36$, $p < 0.01$) and small airways degeneration ($r = -0.28$, $p < 0.01$) were negative and statistically significant. These findings underscore the intricate connections between pulmonary factors and Vitamin D3 levels in COPD, providing valuable insights into potential therapeutic implications. The observed associations and correlations between dysfunctional lung anatomy, small airways degeneration, and Vitamin D3 levels in COPD, align with Persson et al¹⁷ and Janssens et al¹⁸ that highlights the multifaceted interplay between pulmonary factors and vitamin D in chronic obstructive pulmonary disease. Studies by Shaheen et al¹⁹ and Liu et al²⁰ have reported negative associations between vitamin D levels and lung function, supporting our findings of a negative correlation between dysfunctional lung anatomy and Vitamin D3 levels. Moreover, our identified negative correlation between small airways degeneration and Vitamin D3 levels resonates with the work of Dougherty et al,²¹ emphasizing the relevance of small airways in COPD pathogenesis. The beta coefficients and correlation values reported in our study contribute to the growing body of evidence, emphasizing the intricate connections between pulmonary factors and vitamin D in COPD, which may hold therapeutic implications. These results encourage further exploration of targeted interventions aimed at modulating vitamin D levels to potentially impact lung anatomy and small airways degeneration in the management of COPD.

In our study, in the moderate COPD subgroup, the mean Vitamin D3 level was 30.5 ng/mL (SD = 8.2), while in the severe COPD subgroup, the mean was 25.8 ng/mL (SD = 7.5). The observed difference was statistically significant ($p < 0.01$), indicating that individuals with severe COPD had significantly lower Vitamin D3 levels compared to those with moderate COPD. This subgroup analysis underscores the impact of COPD severity on Vitamin D3 levels, emphasizing the potential relevance of Vitamin D3 in the context of disease severity and suggesting avenues for targeted interventions or therapeutic considerations. The observed variation in Vitamin D3 levels based on COPD severity is consistent with existing literature highlighting the intricate relationship between vitamin D status and the severity of COPD. Studies by Persson et

al.¹⁷ and Kunisaki et al.²² have reported lower vitamin D levels in individuals with more severe COPD, aligning with our findings of significantly lower mean Vitamin D3 levels in the severe COPD subgroup compared to the moderate COPD subgroup. The substantial difference in Vitamin D3 levels emphasizes the potential relevance of vitamin D in the context of disease severity, potentially influencing COPD outcomes. These results resonate with research suggesting that vitamin D deficiency may contribute to exacerbations and disease progression in COPD.²³ Our findings contribute to the growing body of evidence supporting the need for further investigation into targeted interventions and therapeutic considerations centered around optimizing Vitamin D3 levels, particularly in individuals with severe COPD.

Study limitations

While our study provides valuable insights, several limitations should be considered. The cross-sectional design hinders establishing causation, emphasizing the need for cautious interpretation of associations. Conducted in a specific medical complex, the generalizability of our findings to diverse populations may be limited. Exclusion criteria, such as pregnant women, might introduce selection bias, and reliance on self-reported data introduces the risk of recall bias. Additionally, the carefully determined sample size, while guiding statistical power, may influence the study's generalizability. Acknowledging these limitations is crucial for a nuanced interpretation of our findings, and future research should address these constraints for a more comprehensive understanding of the relationships between COPD, Vitamin D3, and associated factors.

Conclusion

Our study, involving 189 participants with COPD, aged 40 to 75, revealed significant associations and correlations between dysfunctional lung anatomy, small airways degeneration, and Vitamin D3 levels. Dysfunctional lung anatomy and small airways degeneration exhibited negative associations with Vitamin D3 levels, indicating a potential interplay between pulmonary factors and Vitamin D3 in COPD. Subgroup analyses based on COPD severity demonstrated that individuals with severe COPD had significantly lower Vitamin D3 levels compared to those with moderate COPD. These findings contribute to a nuanced understanding of the complex relationships within COPD, highlighting the importance of considering both pulmonary factors and Vitamin D3 levels in the context of disease severity. Further research and clinical implications may stem from these insights, providing a foundation for tailored interventions and therapeutic strategies in COPD management.

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