International Journal of Basic & Clinical Pharmacology
Patel P et al. Int J Basic Clin Pharmacol. 2026 May;15(3):532-537
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20261120

Original Research Article

Vitamin D3 in severe chronic obstructive pulmonary disease: from profound deficiency to functional recovery

Parth Patel[1], Prathana Patel[2], Krutik Nayak[3]*

[1]Department of Pharmacology, GMERS Medical College, Gandhingar, Gujarat, India
[2]Department of Pathology, B. J. Medical College, Ahmedabad, Gujarat, India
[3]Department of Pharmacology, SMIMER Medical College, Surat, Gujarat, India

Received: 09 March 2026
Accepted: 13 April 2026

***Correspondence:**
Dr. Krutik Nayak,
Email: nayak.krutik@gmail.com

ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is characterized by progressive airflow limitation and systemic inflammation. Vitamin D deficiency is prevalent among COPD patients and correlates with disease severity. This study evaluated the association between serum vitamin D3 levels and COPD severity, and the therapeutic effect of vitamin D3 supplementation.
Methods: A prospective interventional, single-blinded study enrolled 147 COPD patients. Baseline spirometry (FEV1), COPD assessment test (CAT), modified Medical Research Council (mMRC) scores, and serum vitamin D3 levels were recorded. Patients with severe and very severe COPD (GOLD stages 3 and 4, n=58) were randomized into group A (vitamin D3 supplementation) and group B (placebo). Follow-up spirometry and clinical scoring were performed at six months.
Results: Mean serum vitamin D3 levels decreased significantly as GOLD classification increased, from 44.77 ng/ml in GOLD 1 to 18.00 ng/ml in GOLD 4 ($p<0.001$). A strong negative correlation existed between CAT scores and vitamin D levels ($r=-0.822$, $p<0.0001$). Post-intervention, group A showed a highly significant improvement in mean FEV1 from 34.5% to 60.2% ($p=0.001$). Furthermore, vitamin D3 supplementation significantly improved mMRC and CAT scores.
Conclusions: Vitamin D deficiency is profoundly prevalent in advanced COPD. Targeted supplementation in deficient, severe COPD patients significantly improves FEV1, alleviates dyspnea, and reduces overall symptom burden, shifting patients to a moderate disease classification.

Keywords: Cholecalciferol, COPD, Dyspnea, FEV1, Spirometry, Vitamin D3

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder causing massive global morbidity, necessitating a paradigm shift towards predictive, preventive, and participatory health systems that ensure the right intervention reaches the right patient at the right time.[1] Globally, COPD represents a major public health burden, particularly in aging populations and in countries with high exposure to tobacco smoke, biomass fuel, and environmental pollutants. The disease is frequently associated with systemic manifestations such as skeletal muscle dysfunction, osteoporosis, and nutritional deficiencies, which further contribute to functional decline and poor clinical outcomes. This multifactorial medicine approach should be adapted to provide targeted, personalized, and equitable care across diverse populations. Such an evolution would mirror broader biomedical initiatives striving for equitable benefits from genomic and technological advances for individuals of ancestrally diverse backgrounds.[2]

Just as genetic architecture varies across populations, COPD's clinical burden is heavily influenced by a combination of genetics, environmental exposures, and social determinants of health (SDOH). Addressing the complex, multifaceted nature of COPD requires robust knowledge integration through cross-disciplinary collaborations.[3] In the social sciences, interdisciplinarity is essential for synthesizing concepts from multiple domains to explain intricate human behaviors, structural inequalities, and multidimensional phenomena that cannot be understood through isolated lenses.[4] In medical practice, this interdisciplinary approach means moving beyond strict genetic determinism—a concept that risks reducing human beings to their genetic makeup while undermining the role of environment and personal effort, raising profound ethical dilemmas regarding autonomy and the manipulation of human life.[5,6] Instead of viewing diseases purely as immutable genetic destinies, the focus must shift to actionable, holistic precision interventions.

Correcting severe vitamin D3 (cholecalciferol) deficiency in COPD patients represents one such highly accessible and targeted intervention that directly addresses a modifiable clinical risk factor. In recent years, growing attention has been directed toward the role of micronutrient deficiencies—particularly vitamin D—in the pathophysiology and progression of COPD.[7] Vitamin D, traditionally recognized for its role in calcium homeostasis and bone metabolism, is now understood to have broader biological functions involving immune modulation, inflammatory regulation, and skeletal muscle function. The presence of vitamin D receptors in immune cells such as macrophages, dendritic cells, and T lymphocytes highlights its important role in regulating both innate and adaptive immune responses. These mechanisms are particularly relevant in COPD, where chronic airway inflammation and recurrent infections contribute to disease progression and exacerbations.[8]

Vitamin D deficiency is highly prevalent among patients with COPD, with studies reporting deficiency rates ranging from 40% to 80%. Moreover, lower serum vitamin D levels have been consistently associated with increasing disease severity, poorer lung function, reduced exercise capacity, and higher risk of exacerbations. Several mechanisms may explain this relationship, including reduced outdoor activity, chronic inflammation, long-term corticosteroid use, and nutritional deficiencies in patients with advanced disease. Deficiency of vitamin D may exacerbate COPD by promoting airway remodeling, enhancing inflammatory responses, impairing antimicrobial defenses, and increasing susceptibility to respiratory infections.[9]

Looking forward, the strategic use of digital transformation capabilities is poised to further revolutionize COPD management and continuous process improvement.[10] For instance, multimodal machine learning that fuses electronic health records (EHR) with chest X-rays (CXR) provides a holistic framework that significantly improves clinical predictions, particularly for diseases requiring complementary information from both modalities.[11] Furthermore, deploying large artificial intelligence (AI) models in high-stakes vertical systems like healthcare can drastically improve the precision of diagnostic and therapeutic interventions.[12] These clinical models can be further empowered by frameworks leveraging knowledge graph reasoning via reinforcement learning, enabling large language models to perform complex, multi-hop reasoning over dense medical data.[13]

Emerging evidence suggests that correction of severe vitamin D deficiency may have therapeutic benefits in COPD. Clinical trials and meta-analyses indicate that vitamin D supplementation can reduce the frequency of moderate-to-severe exacerbations, particularly in patients with profound baseline deficiency. Additionally, vitamin D may improve skeletal muscle strength, physical performance, and overall functional capacity, thereby contributing to better clinical outcomes.[14]

Given these potential benefits and the need for converging interdisciplinary approach with interventional limitations, investigating the role of vitamin D3 in severe COPD from profound deficiency to functional recovery, it has become an important area of research with implications for both disease management and patient rehabilitation.

Aim and objectives

Aim of the study was to assess the association between vitamin D deficiency and COPD risk.

Objectives were to analyze the level of vitamin D in stable COPD patients as well as severe and exacerbated COPD patients, and to determine the effect of vitamin D supplementation on severe and exacerbated COPD patients.

METHODS

Study design

It was a prospective interventional, single-blinded study.

Study setting

The study was conducted at tertiary care teaching hospital in South Gujarat.

Study period

The study was conducted over a period of 1 year or until the calculated sample size was achieved.

Sample size and technique

The sample size was 147 patients, enrolled using consecutive sampling. The sample size was calculated using Open EPI software.

Inclusion criteria

Patients >18 years of age were included in the study. Patients diagnosed previously or on the spot with COPD based on history, clinical examination, risk factors, and spirometry criteria (FEV1/FVC <0.7 as per GOLD guidelines) were enrolled for the study. Patients willing to give written informed consent were also included in the study.

Exclusion criteria

Hemodynamically unstable patients or those on domiciliary oxygen therapy were excluded. Patients with liver or renal diseases, long-term steroid use, active smokers, alcoholics, or pregnant women were excluded. Patients with diseases affecting vitamin D and calcium metabolism (e.g., osteomalacia, malignancy, thyroid/parathyroid disorders, inflammatory bowel diseases) were excluded. Patients with a history of using drugs that affect vitamin D metabolism, such as Phenytoin, Phenobarbital, Carbamazepine, Isoniazid, Rifampicin, Tenofovir, and Efavirenz were also excluded.

Clinical and biochemical assessments

Baseline demographic data, smoking history, and occupational/chemical exposures were recorded.

Baseline pulmonary function tests (PFTs) were conducted to determine the GOLD classification (stages 1 to 4) based on FEV1 percentage.

Symptom burden and dyspnea were assessed using the COPD assessment test (CAT) score and the modified Medical Research Council (mMRC) grading scale.

Vitamin D3 levels were measured from a random serum sample using chemiluminescence immunoassay (CLIA), with 30-70 ng/ml considered as the biological reference range.

Intervention

Patients identified with severe and very severe COPD (GOLD classifications 3 and 4) were randomly divided into two groups: group A and group B.

Group A received vitamin D supplementation, while group B received a placebo.

Following the intervention, follow-up spirometry readings and clinical scores were noted to determine the treatment's effect.

Statistical analysis

Data was compiled in Microsoft Excel and analyzed using OpenEpi and statistical package for the social sciences (SPSS) version 26.0.

Continuous and discrete variables were analyzed using mean, standard deviation (SD), and percentages.

Intergroup comparisons were carried out using independent t-tests and analysis of variance (ANOVA), while categorical data was assessed via the Chi-square test.

A p value of <0.05 was considered statistically significant, and <0.001 as highly significant.

RESULTS

The study cohort consisted of 147 patients. The demographic data of the participants, detailing age and gender distribution, are presented in Tables 1 and 2. The highest frequency of patients fell in the 50-60 years age bracket (31%), and the study population was predominantly male (80%).

Table 1: Age-wise distribution of patients.

Age group (years)	Frequency	Percentage
20-30	20	14
30-40	41	28
40-50	40	27
50-60	46	31
Total	147	100

Table 2: Gender-wise distribution of patients.

Sex	Frequency	Percentage
Female	30	20
Male	117	80
Total	147	100

According to GOLD spirometric criteria, the baseline distribution was: GOLD 1 (15.6%), GOLD 2 (44.9%), GOLD 3 (23.9%), and GOLD 4 (15.6%). Baseline biochemical profiling revealed that 70% of the subjects had sufficient vitamin D3 levels (>30 ng/ml), 22% had insufficient levels (20-29.99 ng/ml), and 10% were profoundly deficient (10-19.99 ng/ml).

Association of vitamin D with COPD severity

A highly significant progressive decline in mean vitamin D3 levels was observed with worsening COPD severity (Table 3). Patients in GOLD stage 1 had the highest mean vitamin D3 level (44.77±1.71 ng/ml), whereas those in GOLD stage 4 exhibited the lowest (18.00±1.71 ng/ml) ($p<0.001$).

Increased symptom burden also strongly correlated with lower vitamin D3 concentrations (Table 4). Patients with 'very high impact' CAT scores (31-40) had profound vitamin D deficiency (mean 16.50±0.62 ng/ml) compared to those with low impact scores of 0-10 (mean 41.32±4.87 ng/ml). Spearman's correlation analysis confirmed a

strong, highly significant negative correlation between CAT scores and vitamin D3 levels (r=-0.822, p<0.0001).

Table 3: Comparison of mean vitamin D3 level according to GOLD classification.

GOLD classification	N	Mean vitamin D3 (ng/ml)	Standard deviation
1 (mild)	23	44.77	1.71
2 (moderate)	66	35.77	2.22
3 (severe)	35	29.69	3.53
4 (very severe)	23	18.00	1.71
Total	147	32.95	8.33

ANOVA applied, p value <0.001

Table 4: Mean vitamin D3 comparison according to CAT score category.

CAT score category	N	Mean vitamin D3 (ng/ml)	Standard deviation
0-10	35	41.32	4.87
11-20	62	34.84	3.49
21-30	36	27.51	5.58
31-40	14	16.50	0.62
Total	147	32.84	8.35

ANOVA applied, p value <0.001

Impact of vitamin D3 supplementation

Fifty-eight patients in GOLD stages 3 and 4 were randomly divided into the supplementation group (group A, n=29) and the placebo group (group B, n=29). Follow-up after six months revealed that the administration of vitamin D3 resulted in a statistically significant improvement in lung function.

As detailed in Table 5, the mean FEV1 in group A improved markedly from a pre-intervention baseline of 34.5% to 60.2% post-supplementation (p=0.001).

Table 5: Pre- and post-comparison of mean FEV1 for GOLD classification 3 and 4.

Group	N	Pre-treatment mean FEV1±SD	Post-treatment mean FEV1±SD	P value
Group A (vitamin D3)	29	34.50±11.37	60.20±5.65	0.001
Group B (placebo)	29	34.50±11.37	49.40±4.67	0.030

Paired T-test applied

Clinically, supplementation drove substantial improvements in dyspnea. The frequency of patients suffering from severe breathlessness (mMRC grade 3 and 4) decreased significantly following supplementation, correlating directly with improved serum vitamin D levels (Table 6).

Table 6: mMRC grading before and after vitamin D3 supplementation.

Baseline mMRC grade	Frequency pre-supplementation	Frequency post-supplementation	P value
1	32	34	1.000
2	67	70	1.000
3	27	24	0.020
4	21	19	0.001

Paired T-test applied

DISCUSSION

The present study observed a significant prevalence of vitamin D3 deficiency among COPD patients, which correlated inversely with the severity of the airflow limitation. Specifically, the mean vitamin D3 levels exhibited a progressive decline from 44.77 ng/ml in mild COPD (GOLD 1) to a profoundly deficient 18.00 ng/mL in very severe COPD (GOLD 4). This finding suggests that reduced outdoor mobility, systemic inflammation, corticosteroid use, and malnutrition associated with advanced COPD strongly contribute to hypovitaminosis D.

Our findings regarding the progressive decline of vitamin D alongside disease severity align perfectly with multiple previous studies. A 2022 randomized controlled trial by Rafiq et al demonstrated that GOLD 3 and 4 patients had significantly lower serum vitamin D levels compared to those in earlier stages.[15] Similarly, Janssens et al and Khan et al established that vitamin D deficiency becomes more pronounced as COPD progresses; Khan et al specifically noted that the majority of severe and very severe patients exhibited profoundly deficient levels below 20 ng/ml.[16,17] Furthermore, a systematic review by Zhu et al confirmed that the lowest vitamin D levels are universally found in patients in GOLD stages 3 and 4.[9]

The present study also established a strong inverse correlation between vitamin D levels and patient symptom burden, as assessed by CAT scores (r=-0.822) and mMRC dyspnea grades. Patients suffering from the highest symptom impact (CAT scores of 31-40) had the lowest mean vitamin D level of 16.50 ng/ml. This inverse relationship is highly consistent with the findings of Lokesh et al, who found a statistically significant association between high CAT scores (>20) and advanced COPD severity. Furthermore, our observation that higher mMRC grades correlate with severe airflow limitation and low vitamin D matches the findings of Bestall et al who noted that patients with severe COPD frequently present with severe MRC dyspnea scores of 3 or 4.[18]

Crucially, this study evaluated the therapeutic impact of targeted vitamin D3 supplementation in 58 severe and very severe COPD patients over a follow-up period. We observed remarkable clinical and spirometric recovery in the supplemented group compared to the placebo group.

The mean FEV1 in the vitamin D3 group significantly improved from a baseline of 34.5% to 60.2% (p=0.001), effectively shifting these patients to a moderate (GOLD 2) classification.

They concurrently reported statistically significant reductions in breathlessness (mMRC score) and overall symptom impact (CAT score). These interventional outcomes are strongly supported by Khan et al, who concluded that extended vitamin D administration significantly lowers the frequency of acute exacerbations and improves functional capacity in COPD patients.

Additionally, Zhu et al found that high-dose vitamin D supplementation yields significant protective benefits and reduces the severity of the disease specifically in patients with severe vitamin D deficiency.[9,17]

Limitations

While the findings are promising, this study had several limitations.

Sample size and setting

The study was conducted at a single tertiary care center with a relatively small sample size, which may limit the generalizability of the findings to broader populations with different environmental or socioeconomic factors.

Follow-up duration

The 3-month follow-up period, while sufficient to observe initial changes, may be too short to fully assess the long-term impact of vitamin D3 supplementation on disease progression and lung function.

Exacerbation tracking

The study did not directly track the frequency or severity of acute exacerbations during the follow-up period, which is a critical clinical outcome linked to vitamin D levels.

Confounding variables

Factors that can heavily influence vitamin D metabolism and COPD outcomes, such as detailed nutritional status, physical activity levels, and specific comorbidities, were not extensively evaluated.

CONCLUSION

This study demonstrates a strong association between vitamin D deficiency and increased COPD severity. Targeted vitamin D3 supplementation in deficient patients with severe COPD (GOLD stages 3 and 4) provides tangible therapeutic benefits, leading to modest but highly significant improvements in lung function (FEV1), symptom burden, and overall disease stabilization.

Recommendations

Based on these findings, routine screening of serum vitamin D levels should be integrated as a standard aspect of COPD care. Furthermore, vitamin D3 supplementation should be utilized as an effective adjunct therapy for patients with a known deficiency, particularly those in advanced stages of the disease. Future multi-center randomized controlled trials with larger cohorts and prolonged follow-up periods (e.g., 1 year or more) are recommended to fully establish optimal supplementation dosages and properly evaluate the long-term impact on exacerbation rates.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. World Health Organization. Precision medicine: a path towards targeted, personalized and equitable care. 2026. Available at: https://apps.who.int/gb/ebwha/pdf_files/EB158/B158_R2-en.pdf. Accessed on 13 January 2026.
2. Wang Y, He Y, Shi Y, Qian DC, Gray KJ, Winn R, et al. Aspiring toward equitable benefits from genomic advances to individuals of ancestrally diverse backgrounds. Am J Hum Genet. 2024;111(5):809-24.
3. Punjabi S, Misra S, Rippy MA, Grant SB, Galappaththi E, Lim T, et al. A conceptual framework for knowledge integration in cross-disciplinary collaborations. Environ Sci Policy. 2025;172:104197.
4. Sulemana M, Ibrahim A. Interdisciplinarity in the Social Sciences: Conceptual Foundations, Theoretical Perspectives, and Methodological Implications. Volume 4. 2026;4(1).
5. Mishra A. Designer Babies: Ethical, Scientific, and Social Implications. Int J Multidiscip Res. 2025;7(5):53722.
6. Maria W. Navigating the Intricacies of Reproductive Genetics: Ethical Dimensions Explored. J Fertil In vitro IVF Worldw Reprod Med Gent Stem Cell Biol. 2024;12:362.
7. Li X, He J, Yu M, Sun J. The efficacy of vitamin D therapy for patients with COPD: a meta-analysis of randomized controlled trials. Ann Palliat Med. 2020;9(2):286-97.
8. Rafiq R, Aleva FE, Schrumpf JA, Heijdra YF, Taube C, Daniels JM, et al. Prevention of exacerbations in patients with COPD and vitamin D deficiency through vitamin D supplementation (PRECOVID): a study protocol. BMC Pulm Med. 2015;15(1):106.
9. Zhu M, Wang T, Wang C, Ji Y. The association between vitamin D and COPD risk, severity, and exacerbation: an updated systematic review and meta-analysis. Int J Chron Obstruct Pulmon Dis. 2016;11:2597-607.

10. Chang W, Whang JB, Lee JH. The strategic use of digital transformation capability: a meta-analytic approach. Eur J Innov Manag. 2026;16:1-26.
11. Yin K, Xu H, Yao W, Liu C, Chen Z, Cheung YH, et al. When Does Multimodal Learning Help in Healthcare? A Benchmark on EHR and Chest X-Ray Fusion. arXiv. 2026;11.
12. Verma G, Zhou J, Chandra M, Kumar S, Choudhury MD. A Framework for Situating Innovations, Opportunities, and Challenges in Advancing Vertical Systems with Large AI Models. arXiv. 2025;11.
13. Wang S, Yu Y. KG-Hopper: Empowering Compact Open LLMs with Knowledge Graph Reasoning via Reinforcement Learning. arXiv. 2026;11.
14. Kadir Y, Indarta PP. Vitamin D supplementation to reduce chronic obstructive pulmonary disease exacerbation: a scoping review. Int J Adv Med. 2025;12(2):250-6.
15. Rafiq R, Aleva FE, Schrumpf JA, Daniels JM, Bet PM, Boersma WG, et al. Vitamin D supplementation in chronic obstructive pulmonary disease patients with low serum vitamin D: a randomized controlled trial. Am J Clin Nutr. 2022;116(2):491-9.
16. Janssens W, Lehouck A, Carremans C, Bouillon R, Mathieu C, Decramer M. Vitamin D beyond bones in chronic obstructive pulmonary disease: time to act. Am J Respir Crit Care Med. 2009;179(8):630-6.
17. Khan DM, Ullah A, Randhawa FA, Iqtadar S, Butt NF, Waheed K. Role of Vitamin D in reducing number of acute exacerbations in Chronic Obstructive Pulmonary Disease (COPD) patients. Pak J Med Sci. 2017;33(3):610-4.
18. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. Thorax. 1999;54(7):581-6.

Cite this article as: Patel P, Patel P, Nayak K. Vitamin D3 in severe chronic obstructive pulmonary disease: from profound deficiency to functional recovery. Int J Basic Clin Pharmacol 2026;15:532-7.