

Study of Relation between CRP and Vitamin D Level among Copd Patients at a Tertiary Care Center**Kamna Parashar¹, Raju², Arvind Chouhan³, Parag Sharma⁴, Manjula Gupta⁵**¹Post Graduate Resident, Department of General Medicine, Gandhi Medical College & Hamidia Hospital, Bhopal, India²Senior Resident, Department of General Medicine, Gandhi Medical College & Hamidia Hospital, Bhopal, India³Associate Professor, Department of General Medicine, Gandhi Medical College & Hamidia Hospital, Bhopal, India⁴Associate Professor, Department of Respiratory Medicine, Gandhi Medical College & Hamidia Hospital, Bhopal, India⁵Professor & HOD, Department of General Medicine, Gandhi Medical College & Hamidia Hospital, Bhopal, India

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Conflict of interest: Nil

Abstract**Background:** Chronic Obstructive Pulmonary Disease (COPD) is a major health problem worldwide that is characterized by persistent airflow limitation and systemic inflammation. Systemic inflammation and oxidant/antioxidant imbalance have been seen to play a major role in pathogenesis. The present study investigate the level of CRP and vitamin D and its correlation with severity of COPD.**Materials and Methods:** A cross-sectional observational study was conducted over 18 months at a tertiary care center. A total of 100 clinically stable COPD patients and 100 healthy controls were enrolled. Spirometry was performed for diagnosis of COPD and GOLD staging. Serum levels of vitamin D (25-hydroxyvitamin D) and C-reactive protein (CRP) were measured, and erythrocyte sedimentation rate (ESR) was measured. Data were analysed by EPI Info 7.0. P-value of <0.05 was considered statistically.**Results:** The mean age of patients was 56.8±11.2 years and there was a predominance of male patients (90%). According to GOLD staging, 24% had Stage I, 42% Stage II, 22% Stage III and 12% Stage IV COPD. Vitamin D levels progressively decreased with increasing severity (Stage I: 22.95 ± 4.10 ng/mL; Stage IV: 10.05 ± 2.95 ng/mL; p<0.0001) and CRP levels increased significantly (Stage I: 3.62 ± 1.25 mg/L; Stage IV: 10.45 ± 3.05 mg/L; p<0.0001). Vitamin D deficiency was identified in 27% of patients with COPD compared to controls and insufficiency in 70% versus 45% (p<0.0001). COPD patients had significantly higher levels of CRP and ESR than controls (7.49 ± 12.20 vs. 1.28 ± 0.90 mg/L; 28.40 ± 10.20 vs. 4.27 ± 4.50 mm/hr; p<0.0001).**Conclusion:** Vitamin D levels decline and CRP levels increase significantly with worsening COPD severity. Both vitamin D deficiency and elevated inflammatory markers are highly prevalent among COPD patients, highlighting the underlying systemic inflammation and oxidant-antioxidant imbalance in disease pathogenesis. Routine assessment of these parameters may aid in disease monitoring and help guide adjunctive therapeutic strategies.**Keywords:** Chronic Obstructive Pulmonary Disease, Vitamin D, C-reactive protein, COPD severity, systemic inflammation, GOLD staging.**DOI:** 10.25258/ijcpr.18.6.219This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Chronic obstructive pulmonary disease (COPD) is a common, progressive respiratory disease characterized by persistent airflow limitation and chronic airway inflammation. It is a leading cause of morbidity and mortality worldwide and is expected to be the fourth leading cause of death globally by 2030 [1]. Commonly, COPD is

considered a pulmonary disease but it is increasingly recognized that it is a systemic disorder with several extrapulmonary manifestations such as metabolic syndrome, cardiovascular disease and systemic inflammation, all of which contribute significantly to multimorbidity [2]. Approximately, 300 million

people worldwide and is responsible for nearly 3 million deaths each year. The worldwide burden of COPD is predicted to increase further, representing a major public health challenge [2].

Systemic inflammation is one of the main pathogenic mechanisms of COPD pathogenesis and progression. Oxidative stress, caused by a disproportion between reactive oxygen species and antioxidant defenses, has a central role in the pathogenesis of COPD and is closely related to acute exacerbations and disease progression [6].

CRP is an acute phase reactant and a well-established marker of systemic inflammation [3]. It is the most commonly measured inflammatory biomarker and often occurs as an early sign of chronic inflammation in patients with COPD [8]. Various studies have shown that the levels of CRP are significantly higher in COPD patients than in the healthy controls and are positively correlated with disease severity, risk of exacerbation and poor prognosis [4,5].

High CRP has been demonstrated as an important prognostic biomarker, being a strong predictor of hospitalization and death among COPD patients [8]. Both CRP and oxidative stress markers increase significantly in acute exacerbation of COPD (acute state) indicating increased systemic inflammation [6]. Diagnosis is based on clinical investigation and biomarkers. Biomarkers Blood eosinophils, IgE, fibrinogen, procalcitonin, interleukins 6, 8, and 33, tumor necrosis factor alpha, and soluble receptor for advanced glycosylated products (sRAGE) are other inflammatory biomarkers implicated in COPD [7].

Vitamin D has traditionally been known for its role in calcium homeostasis, but has recently been recognized as a pleiotropic hormone with potent immunomodulatory and anti-inflammatory properties [1]. Vitamin D receptors are present in the entire body, and its active form 1,25(OH)₂D₃ can suppress inflammatory signaling pathways, such as NF- κ B and AP-1, which play a crucial role in the pathogenesis of COPD [9]. Vitamin D deficiency is very common in COPD patients and has been associated with a higher risk of disease, increased severity, more frequent exacerbations and reduced lung function [1,2]. Importantly, low vitamin D status has been associated with increased systemic inflammation, as measured by increased CRP levels and other inflammatory cytokines [9,10].

Recent evidence indicates a bidirectional relationship between vitamin D and CRP in COPD patients. Vitamin D deficiency may worsen systemic inflammation, and elevated CRP levels may further inhibit vitamin D metabolism, thus creating a vicious cycle that promotes disease

progression [10]. Studies have revealed a significant negative correlation between serum levels of vitamin D and CRP concentration in COPD patients, which suggests the protective role of vitamin D in the modulation of the inflammatory response [9,11]. However, data regarding the simultaneous assessment of vitamin D and CRP levels in COPD patients especially in Indian tertiary care settings are sparse [12,13].

Thus, the present study was undertaken to determine the relationship between serum CRP and vitamin D levels in COPD patients and to assess their correlation with disease severity at a tertiary care center.

Materials and Methods

The cross-sectional observational study was conducted in the Department of Medicine and the Department of Respiratory Medicine (RIRD), Gandhi Medical College and associated Hospitals (Hamidia Hospital), Bhopal, India, over a period of 18 months. A total of 100 clinically stable COPD patients and 100 age- and gender-matched healthy controls were included in the study. Informed consent was obtained from each participant prior to enrolment, and the study was conducted after approval from the institutional ethics committee.

Inclusion Criteria: Patients aged >18 years, both genders, diagnosed with COPD based on post-bronchodilator FEV₁/FVC ratio <70%, having history of persistent cough, sputum production, dyspnea, and exposure to risk factors, and clinically stable patients (no exacerbation in the preceding 4 weeks) were included in the study.

Exclusion Criteria: Seriously ill patients, inability to properly perform spirometry, patients with congenital or valvular heart disease, patients on vitamin D supplementation, cardiomyopathy or familial hyperlipidemias, patients not willing to participate or not giving consent, and patients <18 years of age were excluded from the study.

Methodology

Sample size was calculated using the formula $n = Z^2 \times p \times q / d^2$, considering a prevalence of COPD in India of 7.4%; at 95% confidence interval and 6% allowable error, the sample size was 100 patients. Spirometry was performed according to ATS/ERS guidelines, and patients were categorized per GOLD staging (Stage I–IV). After overnight fasting, venous blood was collected to analyse Vitamin D (chemiluminescence immunoassay), CRP (immunoturbidimetry), and ESR (Westergren method). A structured questionnaire, clinical examination, spirometry, and laboratory investigations served as data collection tools.

Statistical Analysis: Data were entered in Microsoft Excel and analysed using EPI Info 7.0

software. Continuous variables were expressed as mean $\pm$ standard deviation. Comparison between groups was performed using ANOVA for multiple group comparisons and independent t-test for two-group comparisons.

Categorical variables were compared using Chi-square test. Percentages and proportions were

calculated to determine the significance of the association between Vitamin D and CRP levels with COPD severity. A p-value of less than 0.05 was considered statistically significant.

Observations and Results

Table 1: Baseline Demographic and Clinical Characteristics of COPD Patients

Parameters	Value
Age (years) (Mean $\pm$ SD)	56.8 $\pm$ 11.2
Gender	
Male	90 (90.0%)
Female	10 (10.0%)
COPD Severity	
Stage I	24 (24.0%)
Stage II	42 (42.0%)
Stage III	22 (22.0%)
Stage IV	12 (12.0%)

The study population had a mean age of 56.8 $\pm$ 11.2 years. There was a significant male predominance with 90 (90.0%) patients being male and 10 (10.0%) female. Regarding the severity of COPD, most of the patients were in Stage II (42 cases, 42.0%) followed by Stage I (24 patients,

24.0%). Stage III and stage IV diseases were observed in 22 (22.0%) and 12 (12.0%) patients respectively. The study population was mainly middle aged with a marked male preponderance and moderate COPD severity was the most common stage.

Table 2: Comparison of Vitamin D and CRP Levels According to COPD Severity

COPD Severity	Vitamin D (ng/mL)	CRP (mg/L)
Stage I	22.95 $\pm$ 4.10	3.62 $\pm$ 1.25
Stage II	18.70 $\pm$ 3.85	6.25 $\pm$ 2.10
Stage III	14.10 $\pm$ 3.20	7.85 $\pm$ 2.40
Stage IV	10.05 $\pm$ 2.95	10.45 $\pm$ 3.05
F-Value	41.45	31.19
P-value	<0.0001	<0.0001

The levels of vitamin D were decreasing gradually with the severity of COPD. The highest mean levels were in Stage I (22.95 $\pm$ 4.10 ng/mL) and the lowest levels were in Stage IV (10.05 $\pm$ 2.95 ng/mL). By contrast, CRP levels showed a steady increase with the severity of the disease, increasing from 3.62 $\pm$ 1.25 mg/L in Stage I to 10.45 $\pm$ 3.05

mg/L in Stage IV. The levels of both Vitamin D and CRP varied in different stages of COPD and were statistically significant (F = 41.45 and 31.19 respectively; p < 0.0001) and showed a strong correlation between the severity of the disease and lower Vitamin D level and higher systemic inflammation.

Table 3: Comparison of Vitamin D Status between COPD Patients and Controls

Vitamin D Status	COPD Patients (n=100)	Controls (n=100)	P-value
Deficient	27 (27.00%)	0 (0.00%)	<0.0001
Insufficient	70 (70.00%)	45 (45.00%)	0.019
Sufficient	3 (3.00%)	55 (55.00%)	<0.0001

The levels of vitamin D were significantly lower in patients with COPD compared with the control group. Among the COPD patients, vitamin D deficiency was seen in 27 (27.00%) patients, insufficiency in 70 (70.00%) patients and sufficient in only 3 (3.00%) patients. A deficiency was not observed in the control group. Here, 45 (45.00%) presented with an insufficient vitamin D level and

55 (55.00%) with a sufficient vitamin D status, respectively. All categories were statistically significant. Higher prevalence of deficiency and insufficiency was observed in COPD patients (p < 0.0001 for deficient and sufficient categories; p = 0.019 for insufficient category). Thus, significantly lower vitamin D status was observed in COPD patients as compared to controls.

Table 4: Comparison of Inflammatory Markers between COPD Patients and Controls

Parameter	COPD	Controls	P-value
CRP (mg/L), Mean $\pm$ SD	7.49 $\pm$ 12.20	1.28 $\pm$ 0.90	<0.0001
ESR (mm/hr), Mean $\pm$ SD	28.40 $\pm$ 10.20	4.27 $\pm$ 4.50	<0.0001

CRP and ESR levels were significantly higher in COPD patients than controls. Patients of COPD showed a mean CRP of 7.49 ± 12.20 mg/L and controls showed a mean CRP of 1.28 ± 0.90 mg/L ($p < 0.0001$) which was statistically highly significant. Similarly the mean ESR was significantly higher in COPD patients (28.40 ± 10.20 mm/hr) as compared to controls (4.27 ± 4.50 mm/hr) and this difference was statistically significant ($p < 0.0001$). These results suggest a higher inflammatory burden in COPD patients compared to healthy controls.

Discussion

In the present study, the mean age of COPD patients was 56.8 ± 11.2 years, with the majority belonging to the middle-aged group. There was a marked male predominance with males comprising 90% of the study population. Regarding COPD severity, the majority of patients (42%) had moderate COPD (GOLD Stage II), followed by mild (24%), severe (22%), and very severe (12%). These findings are consistent with previous studies. Patel et al. [14] reported similar demographic patterns in their study of COPD patients, with a mean age of 58.4 ± 9.6 years and male predominance. The higher prevalence of COPD in males can be attributed to greater exposure to risk factors such as tobacco smoking, occupational dust, and environmental pollutants, especially in regions where smoking prevalence remains higher among men.

The present study demonstrated a significant inverse relationship between Vitamin D levels and COPD severity. Vitamin D levels progressively declined from Stage I (22.95 ± 4.10 ng/mL) to Stage IV (10.05 ± 2.95 ng/mL), with the difference being highly significant ($p < 0.0001$). This finding aligns with recent literature. Rus et al. [15] observed that lower vitamin D levels during acute exacerbation were associated with very severe COPD and could serve as a potential clinical indicator of disease severity. Similarly, Sanket et al. [16] in a case-control study reported a significant association between vitamin D deficiency and severity of COPD, with vitamin D levels showing a negative correlation with disease severity. Lokesh et al. [17] also demonstrated that vitamin D deficiency was significantly associated with COPD and its exacerbations, further supporting our findings.

Vitamin D deficiency was observed in 27% of COPD patients in our study, while 70% had insufficiency, and only 3% had sufficient levels.

This is consistent with the findings of Sanket et al. [16] who reported vitamin D deficiency in 32% of COPD patients. The significantly higher prevalence of vitamin D deficiency and insufficiency in COPD patients compared to controls (0% and 45%, respectively) underscores the strong association between COPD and poor vitamin D status. Several mechanisms may explain this association. Vitamin D exerts immunomodulatory effects, and its deficiency has been linked to impaired immune function, increased susceptibility to respiratory infections, and enhanced inflammatory responses. Additionally, reduced sun exposure, poor nutritional status, and chronic inflammation in COPD patients may contribute to vitamin D deficiency.

The present study revealed significantly elevated CRP and ESR levels in COPD patients compared to healthy controls ($p < 0.0001$). CRP levels increased progressively with disease severity, from 3.62 ± 1.25 mg/L in Stage I to 10.45 ± 3.05 mg/L in Stage IV. This is consistent with previous studies demonstrating that CRP levels in COPD patients are not only higher than in healthy individuals but also positively correlate with the severity of COPD. Firouzjahi et al. [18] reported significantly higher serum CRP levels in COPD patients compared to healthy controls, with CRP levels showing a positive correlation with disease severity. Ramya et al. [19] also demonstrated elevated inflammatory biomarkers including CRP and ESR in stable COPD patients, with further elevation during acute exacerbations. These findings confirm that CRP is a valuable marker of systemic inflammation in COPD.

The elevated inflammatory markers observed in our study reflect the systemic inflammatory nature of COPD. Systemic inflammation in COPD arises from the spillover of inflammatory mediators from the lungs into the circulation, leading to various extrapulmonary manifestations. The inverse relationship between vitamin D and CRP levels observed in our study suggests that vitamin D deficiency may exacerbate systemic inflammation, creating a vicious cycle that contributes to disease progression. This is supported by Sanket et al. [16] who found that vitamin D deficiency was associated with increased inflammatory markers and worse clinical outcomes in COPD patients. The strong correlation between vitamin D deficiency, elevated inflammatory markers, and COPD severity underscores the importance of comprehensive assessment in COPD management. Rus et al. [15]

emphasized that vitamin D deficiency is more pronounced in very severe COPD, serving as a potential clinical indicator of disease severity during exacerbation episodes. Lokesh et al. [17] further demonstrated that vitamin D deficiency was associated with increased risk of exacerbations and worse clinical outcomes in COPD patients.

The present study has limitations including single-centre and a small sample size which limits the generalizability and lack of long term follow up. Also, we did not analyse smoking, diet and sunlight exposure as confounders.

Conclusion

This study demonstrates a significant correlation between declining Vitamin D levels, rising CRP levels and worsening COPD severity ($p < 0.0001$). The high prevalence of Vitamin D deficiency and markedly elevated inflammatory markers in COPD patients highlight the role of systemic inflammation and oxidant-antioxidant imbalance in disease pathogenesis. The study highlighted the importance of routine assessment of Vitamin D and CRP may aid in disease monitoring and risk stratification.

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