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# A COMPARATIVE STUDY OF SERUM GAMMA GLUTAMYL TRANSFERASE LEVEL AMONG STABLE AND ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENT AND HEALTHY SUBJECTS

General Medicine

**Dr Shruti Bagaria*** DM Neurology Senior Resident GMC Kota *Corresponding Author
**Dr Amit kumar** Senior Resident in Department of Medicine GMC, Kota, Rajasthan
**Dr Sharda Choudhary** Medical Officer SDH Ossian, Jodhpur, Rajsthan

## ABSTRACT

**Background:** Chronic obstructive pulmonary disease is a progressive respiratory condition characterized by airflow limitation and frequent exacerbations, with gamma-glutamyl transferase emerging as a potential biomarker due to its association with oxidative stress and inflammation. **Methods:** This observational, cross-sectional study was conducted in the OPD and IPD of the Department of General Medicine and Pulmonary Medicine at SMS Medical College, Jaipur. The study included 120 participants: 40 patients with stable COPD, 40 with acute exacerbation of COPD, and 40 healthy controls. Participants aged over 40 years, diagnosed with COPD as per GOLD guidelines, were included. Spirometry testing (pre- and post-bronchodilator) was performed to evaluate pulmonary function ($FEV_1$, FVC, $FEV_1$/FVC ratio). Serum gamma-glutamyl transferase levels were measured, and liver and renal function tests were conducted using blood samples. **Results:** Significant differences in pulmonary function were found across the groups ($P < 0.01$), with the AECOPD group exhibiting the lowest values. Serum GGT levels were highest in AECOPD (31.36 ± 6.10 IU/L), followed by stable COPD (23.80 ± 4.0 IU/L), and control (16.16 ± 3.55 IU/L) ($P < 0.001$). GGT levels correlated significantly with pulmonary function parameters. **Conclusion:** Elevated serum GGT levels are associated with impaired pulmonary function in COPD patients. GGT may serve as a potential biomarker for assessing COPD progression, particularly during acute exacerbations.

## KEYWORDS

COPD, Gamma-glutamyl Transferase, Pulmonary Function, Biomarker, Exacerbation, FVC, FEV, Serum Markers.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common and treatable condition marked by progressive airflow limitation and irreversible lung damage, primarily caused by prolonged exposure to harmful particles, most notably cigarette smoke. This chronic exposure leads to inflammation those results in narrowing airways and reduced lung elasticity, presenting with symptoms such as persistent coughing, shortness of breath, and mucus production[1]. The severity of these symptoms can range from mild discomfort to severe respiratory failure, often exacerbated by acute episodes known as acute exacerbations of COPD (AECOPD) [2]. COPD is currently the third leading cause of death globally, with approximately 90% of these deaths occurring in low- and middle-income countries (LMIC)[3]. In India, the prevalence of COPD is estimated at 7.4% among adults, with COPD accounting for a significant portion of Disability Adjusted Life Years (DALYs). The disease burden in India is particularly high, as it contributes to 75.6% of DALYs related to chronic respiratory diseases[4]. Exacerbations of COPD not only worsen the clinical symptoms but also substantially affect the quality of life, lung function, and overall prognosis of patients, leading to increased healthcare costs and social burdens[5]. Despite advancements in COPD treatment, effective biomarkers to predict or monitor exacerbations remain scarce.[6] Oxidative stress and inflammation are central to the pathophysiology of COPD, with oxidative stress playing a pivotal role in aggravating lung inflammation. Serum gamma-glutamyl transferase (GGT), traditionally used as a marker for liver diseases, is now recognized for its role in oxidative stress[7]. Elevated levels of GGT have been associated with various systemic conditions, including cardiovascular disease, type 2 diabetes, chronic kidney disease, and cancer, further highlighting its potential as a biomarker for COPD and its exacerbations.[8]

This study was aimed to assess the predictive value of GGT in the development of COPD and its correlation with pulmonary function, providing insights into its role as a potential biomarker for monitoring disease progression.

## AIM

To investigate the correlation between serum GGT levels and pulmonary function, and to assess the potential of serum GGT as a biomarker for the progression of COPD.

## OBJECTIVES

To measure serum GGT levels in patients with stable COPD, acute exacerbation of COPD, and healthy controls. And to examine the relationship between serum GGT levels and pulmonary function test results, evaluate the role of serum GGT as a biomarker in the progression of COPD.

## MATERIALS AND METHODS

This cross-sectional observational study was conducted in the OPD and IPD of the Department of General Medicine and Pulmonary Medicine at S.M.S. Medical College, Jaipur, during April 2024 to March 2025

**Study Universe:** The study included COPD patients in stable condition and those experiencing acute exacerbation, along with healthy controls.

**Sample Size:** The sample size was calculated to include 40 subjects in each of the three groups, accounting for an alpha error of 0.05 and a power of 80%. This calculation was based on the minimum detectable difference in serum GGT levels of 5 IU/L, with a standard deviation of 7.2 IU/L.

### Inclusion Criteria

- Aged over 40 years who were diagnosed with chronic obstructive pulmonary disease (COPD)
- Those consented

### Exclusion Criteria

- Participants were excluded if they had pulmonary diseases other than COPD,
- Bronchial asthma, pulmonary tuberculosis, individuals with abnormal liver or biliary tract function, neoplastic pathologies, or any renal or endocrine disorders were not considered for inclusion.
- Regular alcohol consumption was also an exclusion criterion to avoid confounding effects on liver function, particularly serum GGT levels.

**Sampling of Study Population:** All eligible patients were included, resulting in a total sample size of n = 120.

**Statistical Analysis:** Statistical analyses were performed using SPSS software (version 25). For data that were normally distributed with similar variances, a one-way ANOVA was conducted to compare means among the three groups, with Tukey HSD post hoc tests applied for significant findings. ROC curve analysis was conducted to determine the cutoff value for GGT.

## RESULTS

A total of 120 subjects were included in the study and divided equally into three groups: Control (n=40), Stable COPD (n=40), and AECOPD (n=40). The demographic, pulmonary function, and biochemical parameters of the study groups were compared as follows:

**Age and Body Mass Index (BMI)**

The mean age among the Control, Stable COPD, and AECOPD groups was 56.77 ± 8.07, 57.97 ± 8.9, and 58.92 ± 6.8 years, respectively. The differences were not statistically significant (p = 0.488), indicating comparable age distribution across the study groups. Similarly, the mean BMI did not show any significant variation: 21.94 ± 4.2 (Control), 22.29 ± 3.2 (Stable COPD), and 22.17 ± 3.05 (AECOPD), with a p-value of 0.905.

**Pulmonary Function Tests**

Significant deterioration in pulmonary function was observed with progression from Control to Stable COPD and AECOPD. The mean Forced Vital Capacity (FVC) was 3.24 ± 0.22 L in Controls, 2.55 ± 0.32 L in Stable COPD, and 2.01 ± 0.14 L in AECOPD patients (p = 0.000). Similarly, Forced Expiratory Volume in 1 second ($FEV_1$) values were 2.9 ± 0.35 L, 1.96 ± 0.22 L, and 1.04 ± 0.15 L, respectively (p = 0.000). $FEV_1$ percentage ($FEV_1$%) declined progressively with disease severity: 89.8 ± 3.06% in Controls, 78.5 ± 5.17% in Stable COPD, and 42.10 ± 2.13% in AECOPD, showing a statistically significant difference (p = 0.000).

The $FEV_1$/FVC ratio also decreased notably from 90.12 ± 9.44% in Controls to 78.55 ± 16.02% in Stable COPD and 52.12 ± 8.7% in AECOPD (p = 0.000), reflecting an obstructive ventilatory defect. Furthermore, Peak Expiratory Flow Rate (PEFR) values were significantly lower in COPD groups: 487.25 ± 82.51 L/min (Control), 289.25 ± 45.67 L/min (Stable), and 205 ± 22.46 L/min (AECOPD) (p = 0.000).

**Biochemical Parameters**

Serum Gamma-Glutamyl Transferase (GGT) levels showed a marked increase in COPD patients, especially during exacerbation. The mean GGT level was 16.16 ± 3.55 IU/L in Controls, 23.80 ± 4.0 IU/L in Stable COPD, and 31.36 ± 6.10 IU/L in AECOPD, with the difference being statistically significant (p = 0.000). This suggests a possible role of GGT as a biomarker reflecting disease severity and oxidative stress.

Liver enzymes, including Serum Glutamate Oxaloacetate Transaminase (SGOT) and Serum Glutamate Pyruvate Transaminase (SGPT), were also elevated in COPD patients. SGOT levels were 23.45 ± 4.66 IU/L (Control), 27.60 ± 5.01 IU/L (Stable), and 28.53 ± 3.11 IU/L (AECOPD) (p = 0.000). SGPT levels were 21.67 ± 1.5 IU/L (Control), 21.71 ± 3.5 IU/L (Stable), and 25.48 ± 2.6 IU/L (AECOPD) (p = 0.000), indicating hepatic stress or inflammation during acute exacerbation.

**Renal Function Markers**

Urea and creatinine levels increased significantly with disease severity. Mean serum urea levels were 11.11 ± 2.6 mg/dL in the Control group, 24.07 ± 4.09 mg/dL in Stable COPD, and 43.06 ± 8.08 mg/dL in AECOPD patients (p = 0.000). Serum creatinine levels also showed a progressive rise: 0.29 ± 0.12 mg/dL (Control), 0.90 ± 0.02 mg/dL (Stable), and 1.33 ± 0.03 mg/dL (AECOPD) (p = 0.000), suggesting impaired renal function, possibly due to systemic involvement and hypoxia during exacerbations.

**Table. I Comparison of Demographic, Pulmonary Function, and Biochemical Parameters Among Control, Stable COPD, and AECOPD Groups (n = 120)**

| Parameter | Control (n=40) Mean ± SD | Stable (n=40) Mean ± SD | AECOPD (n=40) Mean ± SD | p-Value |
|---|---|---|---|---|
| Age | 56.77 ± 8.07 | 57.97 ± 8.9 | 58.92 ± 6.8 | 0.48 |
| BMI | 21.94 ± 4.2 | 22.29 ± 3.2 | 22.17 ± 3.05 | 0.90 |
| FVC | 3.24 ± 0.22 | 2.55 ± 0.32 | 2.01 ± 0.14 | 0.01** |
| FEV | 2.9 ± 0.35 | 1.96 ± 0.22 | 1.04 ± 0.15 | 0.001** |
| FEV % | 89.8 ± 3.06 | 78.5 ± 5.17 | 42.10 ± 2.13 | 0.001** |
| FEV/FVC% | 90.12 ± 9.44 | 78.55 ± 16.02 | 52.12 ± 8.7 | 0.001** |
| PEFR | 487.25 ± 82.51 | 289.25 ± 45.67 | 205 ± 22.46 | 0.001** |
| GGT | 16.162 ± 3.55 | 23.80 ± 4.0 | 31.36 ± 6.10 | 0.0001** |
| SGOT | 23.45 ± 4.66 | 27.60 ± 5.01 | 28.53 ± 3.11 | 0.01** |
| SGPT | 21.67 ± 1.5 | 21.71 ± 3.5 | 25.48 ± 2.6 | 0.01** |
| Urea | 11.11 ± 2.6 | 24.07 ± 4.09 | 43.06 ± 8.08 | 0.001** |
| Creatinine | 0.29 ± 0.12 | 0.90 ± 0.02 | 1.33 ± 0.03 | 0.01** |

Significance level p <0.05**

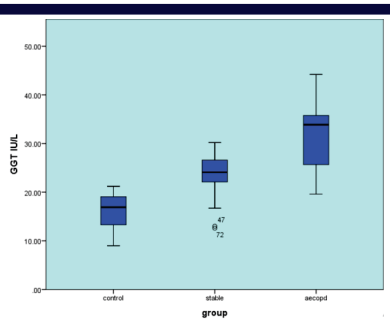


**Fig I. Boxplot Showing Comparison of GGT in Between Control , Stable and AE-COPD Patients.**

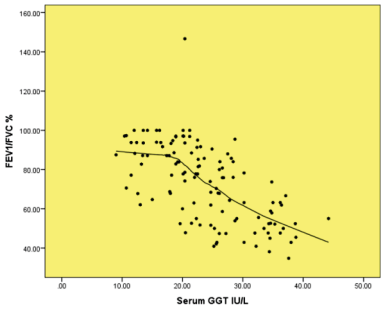


**Fig. II Correlations Between GGT and Forced Expiratory Volume in One Second/Forced Vital Capacity Ratio (FEV1/FVC)**

Our results demonstrates a negative correlation (r = -0.628) between serum gamma-glutamyl transferase (GGT) levels and the $FEV_1$/FVC ratio. As GGT levels increase, the $FEV_1$/FVC percentage decreases, indicating worsening airway obstruction.

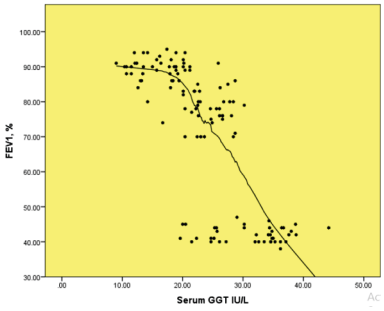


**Fig. III Correlations Between GGT and Forced Expiratory Volume in One Second as the Percentage of the Predicted Value (FEV1%)**

Our results shows strong negative correlation (r = -0.763) between serum gamma-glutamyl transferase (GGT) levels and $FEV_1$% predicted. As GGT levels rise, $FEV_1$% declines, indicating poorer lung function.

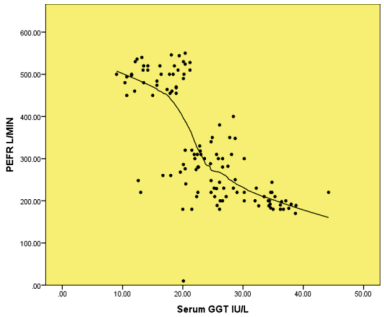


**Fig. IV Correlations Between GGT and Forced Expiratory Volume in One Second as the Percentage of the Predicted Value PEFR L/MIN**

Our study demonstrates a strong negative correlation (r = -0.721) between serum gamma-glutamyl transferase (GGT) levels and peak expiratory flow rate (PEFR). As GGT levels increase, PEFR declines,

suggesting that elevated GGT is associated with reduced respiratory function.

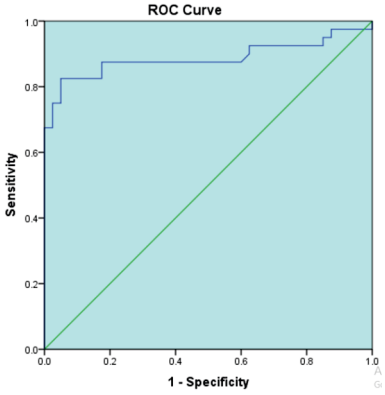


**Fig. V Receiver-operating Characteristic (ROC) Curves for GGT Activity to Evaluate Acute Exacerbation**

Our results shows that The cut-off value for the prediction of acute exacerbation was 28.2 IU/L, with 81 % sensitivity and 89.4% specificity (AUC=0.887; 95% CI, 0.802–0.971; P<0.001).

## DISCUSSION

The mean age of participants was 57.89 years, We found no significant differences between the groups in terms of age, sex, BMI, or smoking history. Our results showed that stable COPD patients had significantly higher GGT levels than healthy controls. Furthermore, GGT levels were notably higher in AECOPD patients compared to those in the stable phase, GGT activity is linked to antioxidant defences during inflammation.[9]

In our study, the control group (n=40) had a mean GGT level of 16.16 ± 3.55 U/L, the lowest among the groups. The stable COPD group (n=40) had a higher mean GGT level of 23.80 ± 4.0 U/L, while the AECOPD group (n=40) showed the highest mean GGT level of 31.36 ± 6.10 U/L. The p-value for GGT comparison across groups was less than 0.001, indicating a significant difference. This suggests that GGT levels rise with COPD severity, with AECOPD patients showing the highest levels. Sun et al[10] demonstrated that a GGT level of 21.2 IU/L can predict COPD diagnosis, and 26.5 IU/L indicates exacerbation.

GGT is often considered a marker of liver damage[11], but no such conditions were present in our study population. Although dietary factors, such as fruit and vegetable intake, and other variables like medication use or alcohol consumption, can influence GGT levels, no significant smoking-related differences were observed across the groups. The link between GGT and lung function remains unclear, though it may reflect oxidative stress, which plays a crucial role in COPD pathophysiology. Elevated GGT activity has been associated with increased oxidative stress and impaired antioxidant systems, which could contribute to airway damage in COPD.

Previous Studies have indicated that excessive oxidative stress can cause transcriptional regulation of inflammatory genes, mucous gland hyperplasia, and irreversible damage to airway epithelial cells.[12-13] Our findings suggest that elevated GGT levels could reflect oxidative stress in COPD, which is consistent with the disease's pathogenesis.

GGT activity was assessed using an ROC curve to determine diagnostic specificity and sensitivity. A cut-off value of 28.2 IU/L was identified for predicting acute exacerbation, with 81% sensitivity and 89.4% specificity (AUC=0.887; 95% CI, 0.802–0.971; P<0.001). The analysis revealed a strong negative correlation between GGT levels and lung function measures. For peak expiratory flow rate (PEFR), the correlation was r = -0.721, indicating that higher GGT levels correspond to lower PEFR. Similarly, GGT had negative correlations with the FEV1/FVC ratio (r = -0.628) and FEV1% (r = -0.763), both reflecting reduced lung function.

In comparison, Sun D et al. found negative correlations between GGT and FEV1% (r = -0.2977) and FEV1/FVC (r = -0.4558), with a cut-off of 26.5 IU/L for acute exacerbation, yielding 69.75% sensitivity and 74.34% specificity (AUC=0.762). Ermis et al. reported a GGT cut-off of 29 U/L for predicting acute exacerbations with 62.8% sensitivity and 70.1% specificity, but they found no significant correlations between GGT levels and various pulmonary function measures.

In our study, significant differences were found in lung function parameters among the control, stable COPD, and AECOPD groups. The AECOPD group had the lowest values: FVC (2.01 ± 0.14 L), FEV (1.04 ± 0.15 L), FEV% (42.10 ± 2.13%), FEV/FVC (52.12 ± 8.7%), and PEFR (205 ± 22.46 L/min), with all comparisons showing P < 0.001.These findings are consistent with studies by Celli et al.[14] which reported similar declines in lung function parameters among COPD patients, and the work of Jones et al.[15] and Sun et al.[10] which further emphasizes the progressive deterioration of respiratory function during exacerbations.

Urea levels are important in COPD as they can indicate kidney function, nutritional status, and the overall severity of the disease, thereby serving as a valuable biomarker in clinical assessments and management of COPD patients. In present study control group (n=40) had a mean urea level of 11.11 ± 2.6 mg/dL, which was the lowest among the groups. The stable COPD group (n=40) showed a notable increase with a mean urea level of 24.07 ± 4.09 mg/dL, while the AECOPD group (n=40) had the highest mean urea level of 43.06 ± 8.08 mg/dL. In line with this, Weng et al.[16] reported mean urea levels of 23.5 ± 6.8 mg/dL in stable COPD patients, increasing to 39.0 ± 7.2 mg/dL during acute exacerbations. Similarly, Garcia et al.[17] found elevated urea levels of 30.2 ± 8.4 mg/dL in COPD patients experiencing exacerbations compared to 20.4 ± 5.1 mg/dL in stable patients. These findings underscore the potential of urea as a biomarker for COPD severity, particularly during acute exacerbations when urea levels are significantly higher.

Assessing creatinine levels in COPD patients is crucial as they serve as indicators of renal function. Elevated creatinine levels may signify renal impairment associated with the systemic effects of COPD, such as chronic inflammation and hypoxia. The control group (n=40) had a mean creatinine level of 0.29 ± 0.12 mg/dL, the lowest among the groups. The stable group (n=40) exhibited a mean creatinine level of 0.90 ± 0.02 mg/dL, significantly higher than the control group. The AECOPD group (n=40) had the highest mean creatinine level of 1.33 ± 0.03 mg/dL. Mather et al.[18] reported mean creatinine levels of 1.1 ± 0.4 mg/dL in COPD patients, suggesting potential renal impairment. Yalcin et al.[19] noted average creatinine levels of 1.2 mg/dL in advanced COPD cases, emphasizing significant renal dysfunction.

This study's findings support this hypothesis, as GGT levels tended to increase with worsening spirometric outcomes. Notably, elevated serum GGT may reflect a chronic, systemic oxidative burden rather than localized pulmonary damage alone, underscoring the systemic nature of COPD.

Serum GGT utility as a biomarker for COPD progression is advantageous for screening and monitoring disease status without necessitating specialized respiratory assessments. Furthermore, incorporating GGT measurement into COPD management could offer additional insights into individual patient profiles, enabling tailored therapeutic interventions to mitigate oxidative stress and slow disease progression.

## CONCLUSION

Our study demonstrated a significant correlation between elevated serum GGT levels and diminished lung function in individuals aged 57 years and in Indian population. This suggests that GGT could serve as a reliable biomarker for assessing the risk of developing COPD and monitoring exacerbations. By identifying patients at higher risk based on GGT levels, healthcare providers could implement early interventions and tailor management strategies to improve patient outcomes, emphasizing the need for further research into GGT's role in respiratory health.

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