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Biochemistry Section

Correlation of Immunoglobulin Free Light Chains in Risk Stratification for Chronic Obstructive Pulmonary Disease Patients: A Cross-sectional Observational Study

R GEETHANJALI[1], MV PREETHI[2], P NIRMALADEVI[3], R GOGULAKRISHNAN[4], V AMUTHAVALLI[5]

ABSTRACT

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality worldwide. Immunoglobulin free Light Chains (IgLCs) have been implicated in various inflammatory diseases; however, their role in COPD risk stratification remains unclear.

Aim: To assess the correlation between IgLC levels and COPD severity and to evaluate their potential role in disease monitoring.

Materials and Methods: This cross-sectional observational study was conducted at Rajiv Gandhi Government General Hospital, Chennai, Tamil Nadu, India, between March and December 2018. A total of 120 stable COPD patients aged over 40 years (post-bronchodilator FEV_1/FVC <70%) with no exacerbations in the preceding three months were included. COPD severity was staged according to the GOLD (Global Initiative for Chronic Obstructive Pulmonary Disease) criteria using spirometry. Venous blood samples were analysed for serum κ and λ free light chains using immunoturbidimetry, along with standard biochemical parameters. Demographic and exposure-related data, including age, sex, Body Mass Index (BMI), smoking status, biomass exposure, and history of tuberculosis, were recorded. Associations between IgLC levels, COPD severity, lung function (FEV_1%), and biochemical parameters were analysed using Pearson's correlation, Analysis of Variance (ANOVA), and Chi-square tests. A p-value <0.05 was considered statistically significant.

Results: The study included 120 COPD patients, comprising 45 (37.5%) males and 75 (62.5%) females, with a mean age of 59.2±10.6 years. The distribution across COPD stages was as follows: 20 (16.7%) in Stage I, 32 (26.7%) in Stage II, 40 (33.3%) in Stage III, and 28 (23.3%) in Stage IV. No significant differences were observed across disease stages with respect to sex, smoking status, biomass exposure, or history of tuberculosis (p-value >0.05). Pulmonary function (FEV_1%) declined significantly with increasing COPD severity, from 82.10±1.21% in Stage I to 26.21±2.45% in Stage IV (F=308.166, p-value <0.0001). Serum κ and λ free light chain levels increased progressively with disease severity (κ: 2.94±0.57 g/L to 5.50±0.81 g/L, F=87.318, p-value <0.0001; λ: 1.50±0.26 g/L to 2.80±0.53 g/L, F=43.616, p-value <0.0001), whereas the κ:λ ratio remained stable across all stages (p-value=1.000).

Conclusion: Elevated IgLC levels showed a strong correlation with worsening COPD severity, declining lung function, and reduced BMI. Despite increases in individual κ and λ light chain concentrations, the κ:λ ratio remained stable across disease stages.

Keywords: Body mass index, Pulmonary function tests, Risk assessment, Smoking

INTRODUCTION

The COPD is a common, preventable, and manageable condition defined by persistent respiratory symptoms and airflow limitation. This limitation results from abnormalities in the airways and alveoli, leading to substantial morbidity and mortality worldwide [1]. Co-morbidities and frequent exacerbations further increase disease severity in affected individuals. In India, COPD affects approximately 5.0% of men and 3.2% of women aged over 35 years [2,3]. Its prevalence increases with advancing age and is influenced by multiple aetiological factors. The Global Burden of Disease Study estimated that by 2020, COPD would become the third leading cause of death worldwide and the fifth leading cause of disability-adjusted life years lost [4,5]. The burden of COPD is particularly high in developing countries, including India, with significantly increased morbidity and mortality. COPD accounts for over half a million deaths annually in India, ranking the country second globally in COPD-related deaths [6].

One of the major risk factors for COPD in developing countries is exposure to smoke from biomass fuel combustion in poorly ventilated indoor environments. In contrast, cigarette smoking is the leading cause of COPD in developed countries. Both exposures induce excessive inflammatory responses within the lungs, leading to obstructive airway disease. The immune response in COPD involves both innate and adaptive immune system components. B cells play a crucial role in adaptive immunity by secreting antibodies that significantly modulate immune responses [7]. During the synthesis of tetrameric immunoglobulins by plasma B cells, an excess of IgLCs is produced relative to heavy chains. These polyclonal free light chains are released into the bloodstream and subsequently cleared by the kidneys, with a half-life of two to six hours. Elevated levels of IgLCs are often associated with increased inflammatory activity, which may contribute to disease progression and worsening clinical outcomes in patients with COPD [8]. The measurement of IgLCs levels in patients with COPD provides a valuable tool for assessing immune responses, stratifying disease severity, and predicting patient outcomes. Understanding the role of these immunoglobulin light chains in COPD pathophysiology may facilitate the development of novel therapeutic strategies. By targeting B cell-mediated pathways, researchers and clinicians may explore new treatment avenues that could improve disease management and prognosis [9].

Examining the immunological mechanisms underlying COPD progression may pave the way for more precise, targeted interventions aimed at reducing inflammation and improving patient

care. In COPD, most inflammatory markers evaluated to date are non specific and are often influenced by comorbid co-nditions. IgLCs, which are produced in excess during B-cell activation, represent a direct marker of systemic immune activation. Although their role has been well established in plasma cell disorders, their relevance in chronic airway inflammation remains poorly studied. In particular, evidence from Indian populations is limited. Assessing free light chain levels in relation to lung function, nutritional status, and disease stage may provide additional information for risk stratification. The present study is novel in correlating both κ and λ free light chains with clinical and biochemical parameters of COPD, thereby addressing an important gap in the existing literature.

This study aimed to evaluate the role of IgLCs in assessing and monitoring COPD severity and to correlate their levels across different stages of the disease as defined by GOLD staging and pulmonary function tests (FEV_1%). The secondary objectives were to evaluate their association with demographic variables, BMI, and biochemical parameters, and to explore their potential role as indicators for risk stratification and disease monitoring in patients with COPD.

MATERIALS AND METHODS

This cross-sectional observational study included 120 patients with stable COPD who attended the outpatient department at Rajiv Gandhi Government General Hospital, Chennai Tamil Nadu, India, from March 2018 to December 2018. Written informed consent was obtained from all participants, and the study was approved by the Institutional Ethics Committee (IEC Reg No: ECR/270/Inst./TN/2013).

Sample size: The sample size was calculated using the formula for correlation studies, assuming an expected correlation coefficient of 0.3, a significance level of α=0.05, and a power of 80%. The minimum required sample size was estimated to be 85. To account for feasibility and potential dropouts, a total of 120 patients were ultimately recruited. The sample size calculation was adapted from Hulley SB et al., [10].

Inclusion criteria: Patients aged over 40 years of either gender with a confirmed diagnosis of COPD (post-bronchodilator FEV_1/FVC <70%) [11] and stable disease, defined as no exacerbation in the preceding three months, were included in the study.

Exclusion criteria: Patients with diagnosed plasma cell disorders, impaired renal function, liver disease, a recent history of hospitalisation for acute exacerbation, ongoing or recent infectious illnesses, or any surgical procedures within the previous three months were excluded. Patients receiving immunomodulatory therapy, including corticosteroids, as well as critically ill patients, were also excluded from the study.

Study Procedure

Participants were classified into four stages of COPD based on lung function (FEV_1%) according to GOLD criteria [11]. Spirometry was performed following standardised protocols. Patient details were entered, and subjects were seated comfortably and instructed to perform forced expiration after full inspiration. COPD was confirmed when the post-bronchodilator FEV_1/FVC ratio was <70%. Blood samples (4 mL) were obtained via venepuncture in a red-capped clot activator tube under aseptic conditions. After 30 mins, the serum was separated by centrifugation (3500 rpm, 10 min, refrigerated). Approximately 0.5 mL was stored at –80 °C for immunoglobulin light chain assay, while the remaining serum was used for urea, creatinine, total protein, and albumin analysis. IgLCs estimation was performed using immunoturbidimetry on a Roche Cobas C501 autoanalyser. In this method, antigen-antibody complexes scatter light in proportion to the concentration of the analyte.

The κ free light chain assay employed anti-κ antibodies to form antigen-antibody complexes, which were measured at wavelengths of 800/340 nm. The reagents consisted of TRIS/HCl buffer (50 mmol/L, pH 8.0), polyethylene glycol (PEG) 7%, and anti-human κ antibody (goat). The assay followed a two-point method with a reaction time of 10 minutes, a sample volume of 3.3 µL, and a reference range of 1.56-4.08 g/L. Similarly, the λ free light chain assay used anti-λ antibodies to form antigen-antibody complexes, measured at 800/340 nm. The reagents included TRIS/HCl buffer (50 mmol/L, pH 8.0), PEG 7%, and anti-human λ antibody (goat). This assay followed a two-point method with a 10-minute reaction time, a sample volume of 4.5 µL, and a reference range of 0.83-2.24 g/L. Calibration was performed using C.f.a.s. Proteins (S1-S6). Quality control was ensured using two levels of control material, with acceptable values maintained within ±2 standard deviations [12,13]. Biochemical analysis included the estimation of total protein using the Biuret method, in which proteins react with Cu^{2+} ions in an alkaline medium to form a purple-coloured complex measured at 540 nm, with a normal reference range of 6-8 g/dL. Serum albumin was estimated using the dye-binding method, wherein albumin binds to bromocresol green (BCG) at pH 4.2 to form a blue-green complex measured at 620 nm, with a normal range of 3.5-5.0 g/dL. Serum creatinine was estimated using Jaffe's kinetic method (IDMS-traceable), in which creatinine reacts to produce a coloured complex measured at 546 nm, with a normal range of 0.5-1.3 mg/dL. Serum urea was estimated using the kinetic urease-GLDH method, in which urea is hydrolysed by urease to ammonia and carbon dioxide; the reaction with α-ketoglutarate and NADH was monitored at 340 nm. The normal reference range for serum urea was 15-40 mg/dL [12,14].

STATISTICAL ANALYSIS

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software, version 24.0. Categorical variables are presented as frequencies and percentages, while continuous variables are expressed as mean±Standard Deviation (SD). Comparisons between two means were performed using Student's t-test, and ANOVA was used to compare more than two means. For variables with significant ANOVA results, Tukey's post hoc test was applied to identify specific pairwise group differences. The Chi-square test was used to assess differences in proportions. Karl Pearson's correlation coefficient was used to evaluate linear relationships between variables. Statistical significance was set at p-value≤0.05. Box-and-whisker plots were used to assess the distribution of immunoglobulin light chains across different stages of COPD.

RESULTS

The study included 120 patients with COPD, comprising 45 (37.5%) males and 75 (62.5%) females. The mean age of the study population was 59.2±10.6 years. The distribution across GOLD stages was 20 (16.7%) in Stage I, 32 (26.7%) in Stage II, 40 (33.3%) in Stage III, and 28 (23.3%) in Stage IV. No significant differences were observed across COPD stages with respect to sex, smoking exposure, biomass exposure, or history of tuberculosis (all p-value >0.05) [Table/Fig-1].

Age (F=1.313, p-value=0.274), BMI (F=1.370, p-value=0.255), blood urea (F=1.183, p-value=0.319), serum creatinine (F=0.943, p-value=0.422), serum albumin (F=1.000, p-value=0.396), and the κ:λ ratio (F=0.002, p-value=1.000) did not differ significantly across COPD stages. In contrast, total protein (F=4.276, p-value=0.007) and albumin-to-globulin (A:G) ratio (F=4.615, p-value=0.004) showed significant differences across disease stages. Pulmonary function, assessed by FEV_1%, declined progressively with increasing disease severity (F=308.166, p-value <0.0001). Serum κ and λ free light chain levels increased significantly with disease progression (κ: F=87.318, p-value <0.0001; λ: F=43.616, p-value <0.0001), whereas the κ:λ ratio remained stable across stages (F=0.002, p-value=1.000). [Table/Fig-2].

Variable	Category	COPD stages				Chi-square value	p-value
		Stage I (n=20)	Stage II (n=32)	Stage III (n=40)	Stage IV (n=28)		
Sex	Male	6 (30.0%)	14 (43.8%)	14 (35.0%)	11 (39.3%)	1.158	0.763
	Female	14 (70.0%)	18 (56.3%)	26 (65.0%)	17 (60.7%)		
Smoking exposure	Yes	13 (65.0%)	14 (43.8%)	19 (47.5%)	13 (46.4%)	2.51	0.602
	No	7 (35.0%)	18 (56.3%)	21 (52.5%)	15 (53.6%)		
Biomass exposure	Yes	10 (50.0%)	19 (59.4%)	21 (52.5%)	16 (57.1%)	0.602	0.896
	No	10 (50.0%)	13 (40.6%)	19 (47.5%)	12 (42.9%)		
Tuberculosis exposure	Yes	15 (75.0%)	14 (43.8%)	19 (47.5%)	19 (67.9%)	10.027	0.124
	No	5 (25.0%)	18 (56.3%)	21 (52.5%)	9 (32.1%)		

[Table/Fig-1]: Demographic and exposure characteristics of COPD patients across disease stages.
Values are expressed as a number (percentage); p-values were calculated using Pearson's Chi-square test (or Fisher's exact test where appropriate); COPD: Chronic obstructive pulmonary disease.

Parameter	COPD stages				F value	p-value
	Stage I (n=20)	Stage II (n=32)	Stage III (n=40)	Stage IV (n=28)		
Age (years)	56.60±8.43	58.41±10.61	60.68±8.93	61.39±10.00	1.313	0.274
BMI (kg/m^2)	23.81±3.38	23.84±4.42	23.08±4.77	21.87±3.06	1.37	0.255
Blood urea (mg/dL)	27.05±10.32	24.56±9.16	27.70±8.69	28.89±9.73	1.183	0.319
Serum creatinine (mg/dL)	0.81±0.41	0.76±0.15	0.84±0.22	0.76±0.20	0.943	0.422
Total protein (g/dL)	6.62±0.82	7.07±0.45	7.09±0.58	7.28±0.75	4.276	0.007
Serum albumin (g/dL)	3.89±0.64	4.08±0.55	3.89±0.53	3.87±0.51	1.000	0.396
A: G Ratio	1.46±0.35	1.42±0.38	1.25±0.31	1.18±0.27	4.615	0.004
FEV1%	82.10±1.21	63.84±7.50	42.18±9.75	26.21±2.45	308.166	<0.0001
Kappa (g/L)	2.94±0.57	3.51±0.45	4.60±0.60	5.50±0.81	87.318	<0.0001
Lambda (g/L)	1.50±0.26	1.80±0.30	2.39±0.55	2.80±0.53	43.616	<0.0001
Kappa-Lambda Ratio	2.00±0.44	2.00±0.39	2.00±0.46	2.00±0.31	0.002	1.000

[Table/Fig-2]: Clinical and biochemical parameters across COPD stages.
Values are presented as mean±standard deviation. p-values were calculated using One-way ANOVA with post-hoc Tukey's test for multiple comparisons; BMI: Body mass index; FEV_1: Forced expiratory volume in one second; FVC: Forced vital capacity; A:G ratio: Albumin to globulin ratio; g/dL: grams per deciliter; mg/dL: milligrams per deciliter; g/L: grams per litre

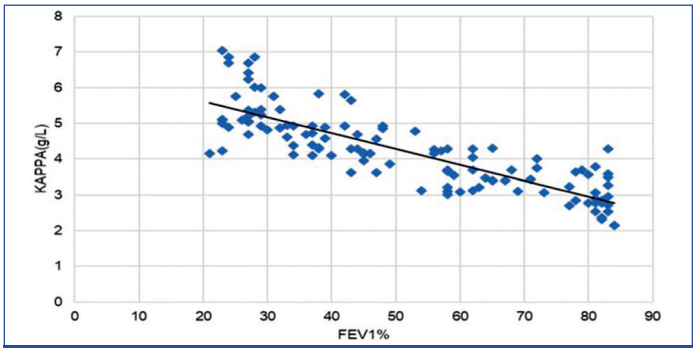
For κ free light chain levels, significant negative correlations were observed with FEV1 (L) (r=-0.648, p-value <0.001), and the FEV_1/FVC ratio (r=-0.880, p-value=<0.001), indicating that higher κ levels were associated with poorer pulmonary function. Additionally, κ showed a weak but significant positive correlation with the κ:λ ratio (r=0.186, p-value=0.042). No significant associations were observed between κ levels and age (p-value=0.959) [Table/Fig-3].

Variable	Age	BMI	FEV_1%	FEV_1 (L)	FEV_1/ FVC	κ:λ ratio
Kappa (g/L)	r=0.005, p=0.959	r=–0.221, p=0.015	r=–0.831, p<0.001	r=–0.648, p<0.001	r=–0.880, p=<0.001	r=0.186, p=0.042
Lambda (g/L)	r=–0.044, p=0.635	r=–0.202, p=0.027	r=–0.721, p<0.001	r=–0.494, p<0.001	r=–0.131, p=0.155	r=-0.451, p<0.001

[Table/Fig-3]: Correlation of κ and λ with clinical parameters.
Values are presented as Pearson correlation coefficients (r) with corresponding p-values (2-tailed); BMI: Body mass index; FEV_1: Forced expiratory volume in one second; FVC: Forced vital capacity; κ:λ ratio: Kappa to lambda ratio; g/L: grams per liter; COPD: Chronic obstructive pulmonary disease

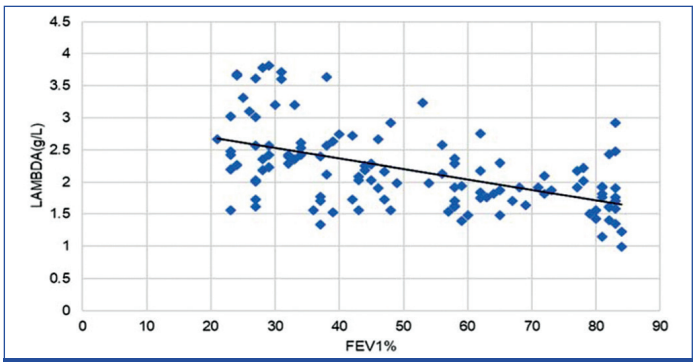
For λ free light chain levels, significant negative correlations were observed with FEV_1% predicted (r=-0.721, p-value<0.001), FEV_1 (r=-0.494, p-value <0.001), FEV_1/FVC ratio (r=-0.131, p-value=0.155), and the κ:λ ratio (r=-0.451, p-value <0.001). These findings indicate that elevated λ levels are associated with worsening lung function and altered light chain balance. No significant correlations were found between λ levels and age (p-value=0.635) [Table/Fig-3].

IgLC κ demonstrated a significant negative correlation with BMI (r=-0.221, p value=0.015). A strong negative correlation was also observed between κ levels and FEV_1% (r=-0.831, p-value <0.001), indicating that higher κ levels were associated with greater airflow limitation [Table/Fig-4]. However, no significant correlation was observed between IgLC κ and age. Similarly, IgLC λ showed a significant negative correlation with BMI (r=-0.202). A strong negative correlation was observed between λ levels and FEV_1% (r=-0.494, p-value <0.001), suggesting that higher λ levels were associated



[Table/Fig-4]: Correlation between IgLC κ and FEV1%.

with greater airflow limitation [Table/Fig-5]. No significant correlation was found between IgLC λ and age.

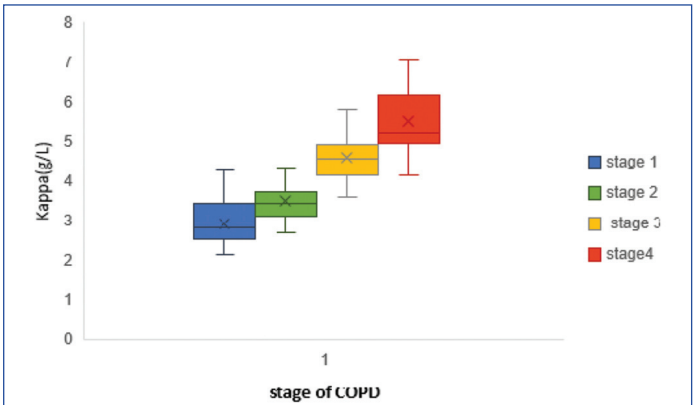


[Table/Fig-5]: Correlation between IgLC λ and FEV1%.

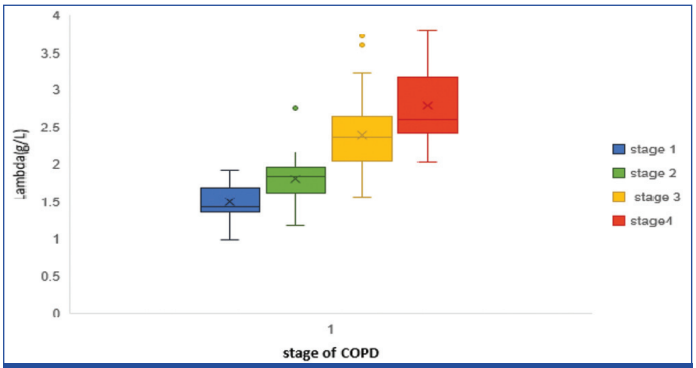
Box-and-whisker plots demonstrated a progressive increase in κ free light chain levels with advancing COPD severity. Median κ levels increased from approximately 3 g/L in Stage I to around 5 g/L in Stage IV, with values exceeding 6 g/L in severe disease. Greater variability was observed in advanced stages, supporting

a significant association between elevated κ levels and disease severity [Table/Fig-6].

Similarly, λ free light chain levels increased progressively with disease severity. Median λ levels rose from approximately 1.5 g/L in Stage I to about 2.5 g/L in Stage IV, with increased variability and outliers in advanced stages, indicating greater dispersion of λ levels in severe COPD [Table/Fig-7].



[Table/Fig-6]: Box and whisker plot showing the distribution of IgLC kappa.



[Table/Fig-7]: Box and whisker plot showing the distribution of IgLC lambda.

DISCUSSION

High IgLC levels were found to correlate with COPD severity, as indicated by reduced FEV_1%. Both κ and λ free light chains increased proportionally, while maintaining a stable κ:λ ratio of approximately 2:1. This pattern suggests systemic immune activation rather than clonal B-cell expansion. Immunoglobulin free light chains may therefore serve as inflammatory markers in COPD; however, their clinical utility should be evaluated alongside established biomarkers such as C-reactive protein (CRP), interleukin-6 (IL-6), and fibrinogen. The stability of the κ:λ ratio further distinguishes COPD-related inflammation from monoclonal gammopathies. Nevertheless, infections and renal dysfunction may influence IgLC concentrations, necessitating careful interpretation of results in patients with COPD [15].

Women were more affected than men across all stages of COPD in the present study, possibly due to greater exposure to biomass fuel combustion and indoor air pollution. This contrasts with earlier studies by Jindal SK, which reported a higher COPD burden among men, primarily attributed to cigarette smoking and occupational exposures [6]. Among the 66 patients with biomass fuel exposure, 37 (56.1%) had severe COPD (Stages III and IV). This proportion was higher than that observed among patients exposed to cigarette smoke (78%), indicating that biomass exposure may be a more significant causative factor in the development and progression of COPD than cigarette smoking in this population [9].

A significant negative correlation was observed between κ and λ free light chain concentrations and FEV_1% (r=-0.831 and r=-0.721, respectively). These findings are in agreement with the study by Braber S et al., which demonstrated elevated IgLC levels in patients with COPD compared with healthy controls. Their study further suggested that IgLCs activate neutrophils, thereby inducing inflammatory responses that exacerbate COPD pathology [16]. Similarly, Caruso C et al., reported significantly higher FLC-κ levels in individuals with asthma compared with control subjects [17]. The present study supports these observations, indicating that elevated IgLC levels may contribute to progressive lung function decline.

Despite increased concentrations of IgLCs, the κ:λ ratio remained constant at approximately 2:1, suggesting proportional immune activation rather than a skewed immune response. This finding was consistent with observations in plasma cell and renal disorders, such as those reported by Pendón-Ruiz de Mier MV et al., where altered κ:λ ratios were indicative of pathological monoclonal processes [18].

A decline in BMI with increasing COPD severity was observed, consistent with findings reported by Guo Y et al., and Park HJ et al., who demonstrated that lower BMI is associated with increased mortality in patients with COPD [19,20]. Guo Y et al.'s meta-analysis revealed a dose-response relationship, with patients having a BMI below 21.75 kg/m^2 exhibiting significantly higher mortality risk [20]. Similarly, Park HJ et al., identified low BMI as a predictor of both COPD development and mortality over a 13-year follow-up period [20]. These findings reinforce the importance of BMI as a prognostic indicator in COPD. Additionally, Sun Y et al., demonstrated a relationship between lower BMI and accelerated FEV_1 decline, further supporting its clinical relevance [21].

An increase in total serum protein with advancing disease severity was observed in the present study, likely attributable to enhanced immunoglobulin synthesis, while serum albumin levels remained unchanged. This contrasts with findings by Incalzi RA et al., who reported hypoalbuminaemia as a common feature in patients with COPD and chronic renal failure [22]. This discrepancy may be explained by the exclusion of patients with recent acute exacerbations in the present study, as exacerbations are known to significantly affect serum albumin concentrations.

A progressive decline in the albumin-to-globulin ratio with increasing COPD severity was also observed, culminating in a reversal at Stage IV disease. This finding aligns with observations by Nilsson U et al., who reported that reduced albumin levels and altered protein ratios were associated with poorer COPD outcomes [23]. Notably, the present study uniquely highlights a potential inflection point in the albumin-to-globulin ratio at advanced disease stages.

Increased serum urea levels were observed in patients with severe COPD, which may reflect chronic systemic inflammation or nephrotoxic effects associated with elevated IgLC levels. Incalzi RA et al., reported a significantly higher prevalence of chronic renal failure in patients with COPD, with concealed and overt renal dysfunction affecting 20.8% and 22.2% of patients, respectively [22]. These findings support the hypothesis that COPD-related systemic inflammation may contribute to renal impairment.

The identified risk factors for COPD in the present study align with findings from previous large-scale investigations by Jindal SK et al., which recognised cigarette smoking, environmental tobacco smoke exposure, and biomass fuel use as major contributors to COPD prevalence [24]. In addition, the meta-analysis by Hu G et al., demonstrated a significantly increased risk of COPD among individuals exposed to biomass smoke (odds ratio=2.44), a factor that was also relevant in the current patient cohort [9].

The role of tuberculosis (TB) in COPD progression, as highlighted by Yakar HI et al., is particularly noteworthy. Their study reported that a history of TB was associated with earlier COPD diagnosis and increased rates of hospitalisation [25]. Although a detailed evaluation of TB history was not undertaken in the present analysis, the potential association between prior TB infection and dysregulated immune activation, as reflected by IgLC levels, warrants further investigation.

The findings of this study suggest that IgLCs may serve as accessible indicators associated with disease severity in COPD. Their observed

relationship with declining lung function and systemic inflammation indicates a potential role in identifying patients with more severe disease phenotypes. Measurement of serum free light chains, in conjunction with established clinical and biochemical markers, may provide clinicians with additional information for monitoring disease progression and guiding management decisions.

Future research should explore the role of IgLCs in the pathogenesis of other chronic inflammatory disorders and assess their concentrations in various COPD-related complications. Furthermore, evaluating antinuclear antibodies and other immunological markers directed against IgLCs may offer additional insights. Therapeutic strategies targeting B-cell-mediated pathways could represent a promising approach for reducing disease progression in patients with elevated IgLC levels. The potential use of free light chain inhibitors, such as F991, in inflammatory diseases also warrants further exploration.

Limitation(s)

The findings of this study require validation in larger, more diverse populations. As the study was conducted in a tertiary care hospital setting, the patient cohort may not fully represent the general population, potentially limiting external validity. Additionally, reference intervals for IgLCs have not yet been established for the Indian population, which may affect the generalisability and clinical interpretation of the results.

CONCLUSION(S)

Serum κ and λ free light chain levels increased significantly with advancing COPD severity and showed a strong negative correlation with FEV_1%, indicating their potential utility as biomarkers of disease progression. The stability of the κ:λ ratio suggests polyclonal immune activation rather than clonal expansion. Estimation of IgLC levels may therefore serve as a useful adjunct to conventional lung function tests in assessing COPD severity and associated systemic inflammation.

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PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Biochemistry, Government Thiruvarur Medical College, Thiruvarur, Tamil Nadu, India.
2. Assistant Professor, Institute of Biochemistry, Madras Medical College, Chennai, Tamil Nadu, India.
3. Associate Professor, Department of Biochemistry, Government Thiruvarur Medical College, Thiruvarur, Tamil Nadu, India.
4. Consultant Specialist, Department of Chest and Thoracic Medicine, Government General Hospital, Karaikal, Tamil Nadu, India.
5. Professor, Institute of Biochemistry, Madras Medical College, Chennai, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. MV Preethi,
Assistant Professor, Institute of Biochemistry, Madras Medical College,
Chennai-600003, Tamil Nadu, India.
E-mail: preethikarthi2627@gmail.com

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