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SERUM NEUTROPHIL TO LYMPHOCYTE RATIO AND HIGH-SENSITIVITY C - REACTIVE PROTEIN LEVELS IN PATIENTS WITH COPD AND THEIR CORRELATION WITH DISEASE SEVERITY

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ABSTRACT **Background:** Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory disorder characterized by persistent airflow limitation and systemic inflammation. Biomarkers such as the Neutrophil-to-Lymphocyte Ratio (NLR) and High-Sensitivity C-Reactive Protein (HsCRP) have been studied for their role in assessing disease severity and predicting exacerbation risks. **Objective:** To evaluate the levels of NLR and HsCRP in COPD patients and analyze their correlation with disease severity to establish their potential as biomarkers for disease monitoring. **Methods:** A cross-sectional study was conducted over two years at the Department of General Medicine, KD Medical College Hospital and Research Centre, Mathura. 70 COPD patients above 40 years were enrolled based on the GOLD criteria. Data were analyzed and Pearson correlation was used to determine the association between biomarkers and disease severity. **Results:** The mean age of participants was 62.94 ± 11.33 years. Stage 3 COPD was most common (44.29%), followed by Stage 2 (24.29%). The mean NLR was 5.47 ± 2.18, and the mean HsCRP was 8.44 ± 2.62. A strong inverse correlation was found between NLR and FEV1 ($r = -0.98$, $p < 0.001$) and between HsCRP and FEV1 ($r = -0.96$, $p < 0.001$). **Conclusion:** NLR and HsCRP are significantly associated with COPD severity, highlighting their potential utility in disease monitoring. Routine assessment of these biomarkers may help reduce hospitalizations and improve patient management. Further studies are needed to validate these findings.

KEYWORDS : Chronic Obstructive Pulmonary Disease (COPD), Neutrophil-to-Lymphocyte Ratio (NLR), High-Sensitivity C-Reactive Protein (HsCRP),Forced Expiratory Volume in1Second (FEV1)

I. INTRODUCTION

Globally, COPD represents a significant public health concern, affecting millions of individuals and contributing to substantial morbidity and mortality rates. Future projections indicate a steady rise in its prevalence over the next ten years[1]. India has an estimated 55.3 million COPD cases, making it the country with the highest COPD prevalence and the second leading cause of death based on disability-adjusted life years. Worldwide, the number of COPD cases is projected to increase due to ongoing exposure to risk factors and a growing elderly population.[2] By 2060, the prevalence rate may result in 5.4 million deaths annually.COPD is now widely acknowledged as a multisystem disorder involving both pulmonary and systemic inflammation. Pulmonary inflammation results from an exaggerated immune response in the lungs triggered by exposure to harmful gases and airborne particles.[3] Smoking is the primary epidemiological risk factor.[4]While tobacco smoking remains the leading cause of COPD, other contributing factors include exposure to indoor and outdoor air pollution (such as dust), occupational hazards like cadmium fumes and grain dust, and genetic conditions like alpha-1 antitrypsin deficiency. In many developing countries, indoor air pollution is a major concern, often resulting from the use of biomass fuels like wood, dry dung, and coal for heating and cooking.The role of systemic inflammation in COPD has driven the search for reliable and easily accessible biomarkers to assess disease activity, predict exacerbations, and guide management. Among these, The Neutrophil-to-Lymphocyte Ratio (NLR) and High-Sensitivity C-Reactive Protein (hs-CRP) have emerged as important markers for assessing systemic inflammation.

The NLR is derived from the ratio of neutrophils to lymphocytes in a standard complete blood count (CBC), making it an inexpensive, readily available, and easy-to-interpret marker of systemic inflammation.[5]Physiologically, neutrophils represent the innate immune system's immediate response to stress, infection, or injury, while lymphocytes are primarily involved in adaptive immune responses. An elevated NLR reflects an imbalance between these two immune cell types, indicating an active inflammatory process.

C-reactive protein (CRP) is another well-established biomarker of systemic inflammation. CRP, an acute-phase reactant synthesized by the liver in response to pro-inflammatory cytokines, serves as a reliable indicator of the body's inflammatory state. Elevated levels of CRP have been consistently observed in COPD patients compared to healthy individuals, with levels correlating positively with disease severity and progression.[6] During AECOPD, CRP levels spike significantly higher than during stable periods, reflecting the heightened inflammatory response associated with exacerbations. This makes CRP a reliable predictor of the occurrence and outcomes of AECOPD.[7]Recently high sensitivity c reactive protein (HSCRP)measuring methods have made it possible to assess this protein in lower levels of inflammation.

II. MATERIALS & METHODS

The research was carried out in the Department of General Medicine at KD Medical College Hospital and Research Centre, Mathura, Uttar Pradesh, used a prospective, cross-sectional design from December 2022 to december 2024, with 70 patients. Inclusioncriteria was patients of COPD (Diagnosed by PFT using GOLD criteria) both males and females >40 year of age, while exclusion criteria included cases of bronchial asthma, pneumonia, bronchiectasis, pulmonary fibrosis, cases of active tuberculosis, any other acute infection, receiving systemic corticosteroids orimmunosuppressive treatment, cases of coronary heart disease, cases of connective tissue disease, cases of chronic kidney disease and endocrine disorders-diabetes, thyroid disease, Cushing's syndrome, Addison disease.

III. RESULTS

Table 1: Distribution of Patients According to Age.

Age Distribution (in years)	No. of Patients	Percentage
40-50	13	18.57
51-60	14	20.00
61-70	31	44.29
71-80	8	11.43
81-90	4	5.71
Total	70	100.00
Mean ± SD	62.94±11.33	

The majority of patients (44.29%) were in the 61-70 years age range, followed by 20.00% in the 51-60 years group and 18.57% in the 40-50 years group. A smaller proportion of patients were aged 71-80 years (11.43%) and 81-90 years (5.71%). The mean age of the patients was 62.94 years with a standard deviation of ±11.33.

Table 2: Distribution of Patients According to COPD GOLD Stage.

GOLD Stage	No. of Patients	Percentage
Stage 1	9	12.86
Stage 2	17	24.29
Stage 3	31	44.29
Stage 4	13	18.57
Total	70	100.00

The largest group comprised patients in Stage 3 (44.29%), followed by Stage 2 (24.29%) and Stage 4 (18.57%). The smallest proportion of patients (12.86%) were in Stage1.

Table 3: NLR Levels Across COPD GOLD Stages

Parameter	Stage 1		Stage 2		Stage 3		Stage 4		P-Value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
NLR	1.63	0.39	3.79	0.84	6.35	0.58	8.22	0.43	<0.001

The mean NLR for Stage 1 was 1.63 ± 0.39, indicating a relatively low level of systemic inflammation. In Stage 2, the mean NLR increased to 3.79 ± 0.84, and in Stage 3, it further rose to 6.35 ± 0.58, reflecting a higher level of inflammation. Stage 4 had the highest mean NLR at 8.22 ± 0.43, suggesting significantly elevated inflammation in severe COPD. The p-value of <0.001 signifies a significant variation in NLR across different stages, emphasizing the rising inflammation with the progression of COPD severity.

Table 4: HsCRP Levels Across COPD GOLD Stages

Parameter	Stage 1		Stage 2		Stage 3		Stage 4		P-Value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
HsCRP	4.01	0.55	6.34	0.48	9.43	0.98	11.9	0.38	<0.001

The mean HsCRP for Stage 1 was 4.01 ± 0.55, indicating a relatively low level of systemic inflammation. In Stage 2, the mean HsCRP increased to 6.34 ± 0.48, and in Stage 3, it further rose to 9.43 ± 0.98. Stage 4 had the highest mean HsCRP at 11.9 ± 0.38, reflecting the highest levels of inflammation in severe COPD. The p-value of <0.001 indicates a statistically significant difference in HsCRP levels across the stages, demonstrating the increasing inflammatory response as COPD severity worsens.

Table 5: Pearson Correlation of NLR with FEV1.

Pearson Correlation	NLR	
	r-value	p-value
FEV1	-0.98	<0.001

There is a strong negative correlation between NLR and FEV1 (r = -0.98, p < 0.001), suggesting that as NLR increases, FEV1 decreases, which is consistent with the worsening of lung function in COPD as inflammation increases. The correlation is statistically significant.

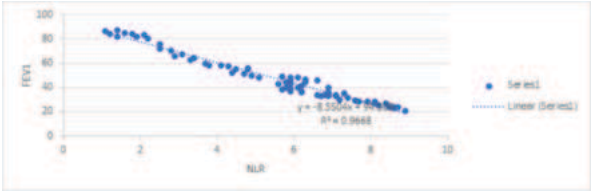
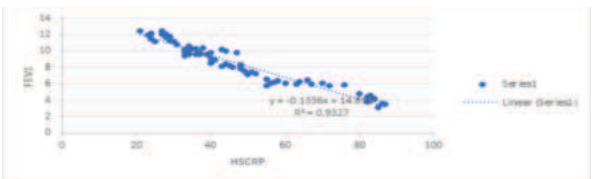


Table 6: Pearson Correlation of HSCRP with FEV1.

Pearson Correlation	HSCRP	
	r-value	p-value
FEV1	-0.96	<0.001

The findings reveal a significant negative correlation (r = -0.96, p < 0.001), indicating that an increase in HsCRP is strongly linked to a decline in FEV1 levels.



IV. DISCUSSION

In our study, the highest proportion of patients (44.29%) belonged to the 61-70 years age group, while 20.00% were between 51-60 years, and 18.57% fell within the 40-50 years range. A comparatively lower percentage of patients were in the 71-80 years category (11.43%), and only 5.71% were aged 81-90 years. The overall mean age of patients was 62.94 years, with a standard deviation of ±11.33.

Similarly, Moayyedkazemi A et al[8] reported a mean age of 66.98±10.3 years in the COPD group, while the control group had a mean age of 66.02±8.7 years, indicating that both groups were well-matched in terms of age. In contrast, Zhao T et al[9] found the average age of COPD patients to be 71.34 ± 11.51 years.

The mean NLR values across GOLD stages in our study demonstrated a significant increase in systemic inflammation as COPD severity progressed ($p < 0.001$). Stage 1 had the lowest mean NLR at 1.63 ± 0.39, while Stage 2 showed a moderate rise to 3.79 ± 0.84. In Stage 3, NLR further increased to 6.35 ± 0.58, and Stage 4 had the highest level at 8.22 ± 0.43, indicating significantly elevated inflammation in severe COPD.

Similarly, Bilir B et al[10] observed that NLR values increased with disease progression, ranging from 1.64 in Stage I (stable) to 3.7 in Stage IV (exacerbation), with a statistically significant difference ($p < 0.001$). Sakurai K et al[11] also found a rising trend in NLR across GOLD stages, reporting values of 1.9 (1.4–2.4) in Grade 1, 2.1 (1.5–2.6) in Grade 2, 2.3 (2.0–3.0) in Grade 3, and 2.7 (1.9–5.3) in Grade 4, reinforcing the link between COPD severity and systemic inflammation.

The mean HsCRP values in our study demonstrated a significant increase in systemic inflammation with COPD progression ($p < 0.001$). Stage 1 had the lowest mean HsCRP at 4.01 ± 0.55, while Stage 2 showed a moderate increase to 6.34 ± 0.48. In Stage 3, HsCRP further rose to 9.43 ± 0.98, and Stage 4 had the highest level at 11.9 ± 0.38, reflecting the most severe inflammatory response in advanced COPD.

Similarly, Moayyedkazemi A et al[8] found a significant correlation between COPD severity and HsCRP levels, reporting a correlation coefficient of $r = 0.315$ ($p = 0.048$). This further supports the association between increasing systemic inflammation and disease progression in COPD.

A strong negative correlation was observed between NLR and Forced Expiratory Volume in with decreased Forced Expiratory Volume in 1 second (FEV1). The strong negative correlation ($r = -0.98$, $p < 0.001$) implies that as NLR increases, lung function declines significantly. with declining lung function in COPD, reinforcing the link between inflammation and disease progression.

Sari A P et al[12] similarly reported a negative correlation between NLR and FEV1, with r = -0.6 in acute exacerbation COPD (AE-COPD) and r = -0.54 in stable conditions.

Yousef A M et al[13] reported an inverse association between NLR and airflow limitation, with a Pearson correlation coefficient of -0.148 ($p < 0.001$), indicating that higher NLR levels correlate with worse pulmonary function. Moayyedkazemi A et al[8] found negative correlations between hsCRP and COPD severity, with r = 0.035 in COPD patients and r = 0.001 in the control group.

V. CONCLUSION

Frequent and severe exacerbations of COPD not only worsen the patient's health status but also accelerate disease progression and increase mortality risk. Early identification of exacerbations is crucial for timely intervention and improved patient outcomes. The results of this study underscore the importance of inflammatory biomarkers, including the Neutrophil-to-Lymphocyte Ratio (NLR) and High-Sensitivity C-Reactive Protein (HsCRP), in forecasting COPD exacerbations. Both biomarkers show a marked increase during exacerbations, indicating their potential role in early detection. Incorporating these biomarkers into routine clinical assessments may aid in proactive disease management, reduce hospitalization rates, and ultimately improve the quality of life for COPD patients. Further large-scale studies are warranted to validate their utility in clinical practice.

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