



“Study of Neutrophil to Lymphocyte Ratio in Acute Exacerbation of Copd Patients”

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ABSTRACT

Objective:-Increased inflammation in lungs is associated with raised inflammatory markers in circulation leading to an increase in systemic inflammation. Several inflammatory biomarkers which are found to be raised in COPD one of them is Neutrophil to lymphocyte ratio (NLR). NLR is a useful systemic inflammatory response biomarker that is calculated from Complete Blood Count (CBC) and this study was done to evaluate the correlation between neutrophil to lymphocyte ratio and severity of COPD.

Methodology :- This prospective observational study was conducted on patients attending Netaji Subhash Chandra Bose Medical College & Hospital, Jabalpur during the study period (August 2022 to February 2024). A sum total of 110 patients with Chronic Obstructive Pulmonary was included in the study, out of which 70 cases were with AECOPD and 40 cases were with stable COPD. NLR was calculated from a peripheral blood sample of the study participants. Continuous variables were summarised as mean with standard deviation and compared between groups using Unpaired t-test. A p-value <0.05 was considered statistically significant.

Result:-Mean level of NLR in AECOPD is 4.8 ± 1.7 compared to 2.3 ± 0.8 in stable COPD which was statistically significant. A linear increase was observed in NLR with AECOPD severity, which may show the relationship between increased NLR and severity of AECOPD. (statistically significant in both the groups P value <0.001 in AECOPD group and <0.022 in stable COPD). Poor outcome was seen in patients of acute exacerbated COPD as compared to stable COPD.

Conclusion:-We concluded that NLR is an inflammatory biomarker that rises significantly during AECOPD and can be used to predict COPD exacerbations and severity of COPD. Those who have more the value of NLR indicate more severe disease. The prognosis and survival is poor in high NLR ratio patients. This study shows higher NLR in non-survivor patients of AECOPD and thus can

be promising prognostic marker for assessing in-hospital mortality in patients with AECOPD.

I. INTRODUCTION

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is one of the leading causes of hospitalization and contributes significantly to mortality among patients of COPD.[1]

AECOPD has an independent and significant negative influence on the prognosis of patients with COPD. It increases the frequency of further severe exacerbations, reduces health status and physical activity, speeds the decline of lung function, increases mortality and places great economic burden in patients of COPD[2]. Increased inflammation in lungs is associated with raised inflammatory markers in circulation leading to an increase in systemic inflammation [3]. Several inflammatory biomarkers which are found to be raised in COPD are C-Reactive Protein (CRP), Interleukin-8 (IL-8), Tumour Necrosis Factor (TNF- α), leptin, endothelin-1, fibrinogen, IL-6, Leukotriene (LT) B4 and E4[4] Although some of these novel biomarkers can identify the severity of disease and acute exacerbation in COPD, most of them are time-consuming, expensive, and not readily available [5].

The Neutrophil-Lymphocyte Ratio (NLR) is a rapid, easy and cheap biomarker that is calculated from Complete Blood Count (CBC). NLR can detect the inflammatory status during acute exacerbations of COPD (AE-COPD) and could identify early acute exacerbations for early management. So we evaluated the correlation between neutrophil to lymphocyte ratio and severity of COPD.

II. MATERIAL AND METHODS

- This study was an observational study over a duration of 18 months (August 2022 to feb 2024) carried out in NSCB Medical college and hospital Jabalpur after taking approval and consent from ethical committee. A sum total of



110 patients with Chronic Obstructive Pulmonary Disease attending Netaji Subhas Chandra Bose Medical College & Hospital were included in the study, based on the inclusion and exclusion criteria. The study was done after getting informed & written signed consent from the patients participating in the same. The study includes patients with Chronic Obstructive Pulmonary Disease irrespective of the severity and duration of disease.

Inclusion criteria

- Patients admitted in NSCBMEDICAL COLLEGE AND HOSPITAL JBP with acute exacerbation of COPD and stable COPD.

Exclusion criteria

- Patients of Bronchial Asthma, Bronchiectasis or Bullous lung disorders.
- Patients with pulmonary tuberculosis.
- Patients with lung malignancy.
- Patients with hepatic disease, renal disease, myocardial infection.
- Patients with any other acute or chronic infections.
- Patients receiving systemic corticosteroids, antibiotics, immunosuppressive treatment.

Investigations

COMPLETE BLOOD COUNT (CBC), TLC, DLC (including neutrophil and lymphocyte counts), Hemoglobin, Random blood sugar, Blood urea, Serum creatinine, Serum electrolytes, Sodium, Potassium, CXR, Sputum AFB, PFT, (CT Chest, Sputum culture and Sensitivity when ever needed).

Tools used

Detailed History of symptoms, Clinical examination, NLR, PFT, Chest xray, Baseline demographic data need to be obtained like:

- Age and Gender, risk factors (history of smoking, exposure to air pollution, working with chemicals, dust, history of childhood respiratory infection,) , Laboratory data (CBC, WBC, NLR,) was entered into a checklist. .

All measurements were performed after blood collection at Central Pathology Lab of NSCBMCH Jabalpur by an automatic cell counter.

(Echo cardiographic examinations was performed in Cardiology Department at Super Speciality Hospital Jabalpur whenever needed.)

III. DATA COLLECTION

Statistical analyses was performed using SPSS version 15.01. Independent-sample t-test, paired t-test and Mann-Whitney U tests were used for the comparison of continuous variables.

Pearson's correlation was used between NLR and other inflammatory markers. Receiver operating characteristic (ROC) curves was constructed for the WBC, NLR, and other variables and the areas under the ROC curve values with 95% CIs was calculated and compared with each other. Optimal cut-off values was determined; sensitivity, and specificity was calculated with (95% CI). P value < 0.05 was considered statistically significant.

DATA ANALYSIS PLAN

- All the records were recorded by using structured schedule (case Report form)
- Detailed medical and surgical illnesses history and clinical, physical examination of both study groups were carried out.
- Patient's (cases) peripheral blood smear (NLR) were taken and their PFT recordings were recorded .
- All the data was recorded using structured schedule (case report form) and entered for tabulation in Microsoft Excel Sheet.
- Statistical analysis was performed using SPSS version 15.
- Independent-samples t-test, paired t-test and Mann-Whitney U tests were used for the comparison of continuous variables. Pearson's correlation was used between NLR and other inflammatory markers. Receiver operating characteristic (ROC) curves was constructed for the WBC, NLR and other variables and the areas under the ROC curve values with 95% CIs was calculated and compared with each other. Optimal cut-off values was determined; sensitivity, and specificity was calculated with (95% CI). P value < 0.05 was considered statistically significant .
- Master chart and proforma was attached and collected data was statistically analysed using EPI-INFO software .

EXPECTED OUTCOME NLR can be good inflammatory and prognostic marker for COPD Exacerbation patients.

FINANCIAL SUPPORT-NIL

SPONSORSHIP-NIL

CONFLICTS OF INTEREST-There are no conflicts of interest.

IV. RESULT

After approval by Institutional Ethical Committee and written informed consent a total 110 cases were selected, out of which 70 cases were with AECOPD and 40 cases were with stable COPD.



Various parameters such as age, sex, occupation, smoking index, neutrophil, lymphocyte, NLR, oxygen requirement, death and discharge were studied.

In present study mean age (Table 1) of AE-COPD was 61.57± 9.25 years whereas, the mean age for stable COPD was 57.9 years.

Majority of the patients were (Table 1) male (77%) in AECOPD group and stable COPD

group (72.5%) as compared to females which was (33%) in AECOPD and (27.5%) in stable COPD.

The occupational based distribution of patients in present study were found that majority of patients were labourers (44.5%) followed by housewives (19.1%) then businessmen (18.2%) and farmers (18.2%).

Table 1 :- Demographic details

PARAMETER		AECOPD	Stable COPD
Age(mean ±SD)		61.57±9.27	57.9±27
Gendar	Male	77%	77.5%
	Female	33%	27.5%

Smoking status distribution of the sample population measured in pack-years. Of the respondents, 32 (29.1%) reported 0 pack-years, 2 (1.8%) reported less than 10 pack-years, 12 (10.9%) reported 10-20 pack-years, 48 (43.7%) reported 21-30 pack-years, and 16 (14.5%) reported more than 30 pack-years.

Mean level of NLR (Table 2) in AECOPD is 4.8±1.7 compared to 2.3± 0.8 in stable COPD which was statistically significant. A linear increase was observed in NLR as Gold grading increases in both the groups.

Stable COPD and AECOPD patients were classified according to the (graph 1) GOLD criteria.

A linear increase was observed in NLR with AECOPD severity, which may show the relationship between increased NLR and severity of AECOPD. (statistically significant in both the groups P value <0.001 in AECOPD group and <0.022 in stable COPD.)

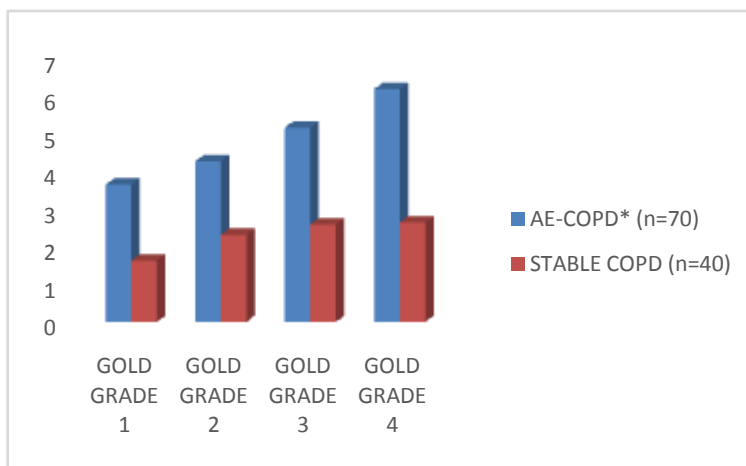
Poor outcome (table 4) was seen in patients of acute exacerbated COPD as compared to stable COPD. Out of 70 patients in AECOPD, 58 (82.8%) patients were discharged and (17.2%) patients died whereas 100% discharge rate was seen in stable COPD group and no death occurred.

Table 2 :NLR ratio in AECOPD and STABLE COPD group

PARAMETER	AECOPD (mean % ± SD)	STABLE COPD GROUP (mean % ± SD)	P VALUE
NEUTROPHIL	80.1 ± 4.1	69.4± 5.7	<0.001
LYMPHOCYTE	17± 4.2	25.6 ±3.4	<0.001
MEAN NLR	4.8±1.7	2.3.±0.8	<0.001
TOTAL	70	40	

***AE-COPD: Acute Exacerbation COPD**

Table 2 shows that, Neutrophils and NLR ratio is significantly higher in the AECOPD group as compared to COPD group. P value (<0.001).



Graph 1 : Distribution of GOLD grading along with NLR and severity of the COPD.

Graph 1 :- shows a linear increase was observed in NLR with AECOPD severity.(statistically significant in both the groups P value <0.001 in AECOPD group and <0.022 in stable COPD.

Table 3 : Distribution of Outcome of COPD according to their diagnosis status (n=110)

VARIABLE	AECOPD(n=70) N (%)	STABLE COPD(n=40) N(%)
DEATH	12 (17.8%)	00
DISCHARGE	58 (82.2)%	40 (100%)
TOTAL	70	40

Table3 stated that poor outcome of death was seen in patients of acute exacerbated COPD as compared to stable COPD. Similarly, out of 98 discharged patients, 58(59.2%) were AE- COPD patients whereas 40(40.8%) were stable COPD patients. Moreover, Disease outcome with AECOPD severity was found to be statistically highly significantly associated (**chi-square value: 7.697; p-value:0.006**).

V. DISCUSSION

COPD is a progressive disease which is complicated with acute exacerbations. It has been a prevalent health problem and also an economical burden.

The current study was conducted to evaluate neutrophil to lymphocyte ratio in COPD patients and to correlate neutrophil to lymphocyte ratio with severity of COPD.

NLR RATIO IN COPD PATIENTS

In our study we found that NLR during Acute exacerbation in COPD patients was higher compared to the stable COPD. NLR as a marker in patients with stable COPD and AECOPD has been evaluated in the past few years Similar findings have been reported by a number of studies.(Table no 4).

Table no 4 :- Summary of findings in the current study and previous similar studies

PARAMETER	AECOPD	STABLE	P-value
NLR(mean±SD)			
CURRENT STUDY	4.8±1.7	2.3± 0.8	<0.001
GUNAY ET AL[6]	4.28±4.12	2.59±1.79	<0.001
LEE ET AL[7]	12.4±10.6	2.4±0.7	<0.001
XIONG ET AL[8]	4.88±1.84	2.02±1.92	<0.001
TAYLAN ET AL[5]	7.1±5.4	3.1±2.5	<0.001



CORELATION OF NLR WITH SEVERITY OF COPD

A linear increase was observed in NLR with COPD severity, which may show the relationship between inflammation and increased NLR in both the groups. As severity increases, NLR increases.

Similarly **FURUTATE et al.**[9] found that NLR was significantly correlated with the forced expiratory volume in 1 s (FEV1). **BILIR et al** [10] found A linear increase was observed in NLR with COPD severity and found non linear pattern in AECOPD. **YASAR et al** [11] detected a negative correlation between NLR and FEV1. **LEE et al**[12]. performed a wider study enrolling 885 patients and found that As the NLR quartile increased, respiratory functional parameters (FEV1, FVC, and FEV1/FVC) significantly deteriorated. **LEE et al**[7] found the correlations between NLR and FEV1 , in 33 patients with stable COPD and eight with AECOPD, it was found that associations with FEV1 were not significant.

The relation of NLR with pulmonary functions has not been sufficiently examined in the literature. In our study, A negative correlation was detected between NLR level and both FVC and FEV1 levels in stable COPD and AECOPD. These results mean that the more severe the COPD is, more is the NLR and more severe is the inflammation. So the NLR could be a practical marker to estimate inflammation severity.

OUTCOME OF THE PATIENTS

Present study shows that poor outcome is seen in acute exacerbated COPD patients with high NLR as compared to stable COPD who had low mean NLR. **RAHIMIRAD et al.** [13] retrospectively reviewed 315 hospital charts of COPD patients. NLR values were higher in AECOPD patients who died in hospital than in those discharged alive. Retrospective study done by **YAO et al.**[14] found that NLR values were significantly higher in patients who died in hospital than in those who survived. **SHARMA et al.**[15] retrospectively studied 181 patients with AECOPD . Death occurred in 16 (9%) patients within 90 days and in 32 (18%) patients within 12 months from discharge. The mean NLR values were higher in patients who died than those of survivors.

VI. LIMITATION

This study had certain limitations. Firstly, it is a single center study and relatively small sample size, which limits generalising our findings. Secondly we did not evaluate data like COPD evaluation test and BODE index, thus the

patients could not be classified into recent COPD classification

VII. CONCLUSION

This study elucidated that NLR is an inflammatory biomarker that raises significantly during AECOPD and can be used to predict COPD exacerbations and severity of COPD. Those who have more the value of NLR indicate more severe disease. The prognosis and survival is poor in high NLR ratio patients. This study suggests higher NLR in non-survivor patients of AECOPD and thus can be promising prognostic marker for assessing in-hospital mortality in patients with AECOPD.

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