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Neutrophil-Lymphocyte Ratio as a Marker of Disease Severity and Exacerbation in Chronic Obstructive Pulmonary Disease Patients: A Cross-Sectional Study

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Abstract

The hallmark of chronic obstructive pulmonary disease (COPD) is a persistent and irreversible restriction of airflow that is accompanied by an increased chronic inflammatory response of the lungs and airways to harmful gases and particles. Acute exacerbations, which are one of the defining characteristics of COPD, are frequently accompanied by an increase in inflammation brought on by infections or even environmental factors. Counting leucocytes and identifying their subtypes are common indicators of inflammation. For clinical outcomes in COPD patients, neutrophil to lymphocyte ratio (NLR) is regarded as an inflammatory biomarker. This study aimed to determine the predictive value of the neutrophil to lymphocyte ratio in patients with stable disease and acute exacerbation of chronic obstructive pulmonary disease Materials and Present study was a prospective cross-sectional study conducted in Department of General Medicine, Sree Mookambika Institute of Medical Sciences, Kulasekharam for a period of one year. A total of 80 patients with acute exacerbation of COPD and stable COPD patients were included in the present study. Clinical data were collected. Degree of dyspnoea was assessed using Modified Medical Research Council (MMRC) dyspnoea scale. Pulmonary function tests were done. Blood samples were collected from the patients for total WBC count, differential WBC count and for absolute neutrophil and lymphocyte count. Neutrophil-to lymphocyte ratio was calculated by dividing absolute neutrophil count by absolute lymphocyte count. Results were analysed using SPSS 20.0 version and the association was tested using one-way ANOVA and Chi square test. COPD is more prevalent among smokers and male gender. In the present study 15(18.75%) had NLR between 0 to 2.5, 21(26.25%) had NLR between 2.6 to 5, 35(43.75%) had NLR between 5.1 to 7.5, 9(11.25%) had NLR between 7.6 to 10. NLR correlated with the severity of airflow obstruction. NLR has a positive correlation with MMRC scale. Mean NLR was significantly higher in COPD exacerbation compared to patients with stable COPD. With its rapid, inexpensive, and easily measurable feature with normal complete blood count analysis, NLR could be thought of as a novel inflammatory marker for assessing inflammation in COPD patients. All COPD patients should routinely employ NLR as a prognostic marker of mortality. NLR may serve as a marker for COPD exacerbations.

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Key Words

Chronic obstructive pulmonary disease, dyspnoea scale neutrophil, lymphocyte

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major health-care concern around the world[1]. COPD is characterised by symptoms of ongoing airflow restrictionits aggravation is linked to a generalised airway inflammatory response. Extra pulmonary symptoms include systemic inflammation, malignancies, cardiovascular disease, cachexia and muscular disorders, osteoporosis, anemia, anxiety depression, which are frequently linked to COPD[2].

Hospitalisation, a decline in quality of life an increase in mortality are all strongly correlated with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). A prompt identification of AECOPD therefore seems essential to avoiding the previously mentioned complications[3].

Low-grade persistent systemic inflammation is a hallmark of COPD number of biomarkers, including C-reactive protein (CRP), IL-6surfactant protein D (SPD), have been linked to an elevated likelihood of death in COPD patients. Although numerous systemic inflammatory biomarkers have recently been tested to identify some characteristics of COPD, their clinical application is hindered by high costs and technical issues[4].

Inflammation may play a role in numerous cell types in COPD, including neutrophils, macrophages, as well as lymphocytes. Reactive oxygen species (ROS) along with neutrophil elastase in particular are important sources of proteases and are indicators of acute inflammation[5]. In this respect, the blood neutrophil-to-lymphocyte ratio (NLR) has been demonstrated to be a useful predictor of inflammatory illnesses and is utilised for risk stratification of several diseases including COPD, pancreatitis, acute coronary syndrome, sepsis infectious diseases. This index is a quick, simple affordable approach that is calculated from a standard complete blood count used in clinical practise[6].

NLR represents the ratio of neutrophils to lymphocytes, which stand for both the innate as well as adaptive immune systems, respectively. Changes in the immune system and the inflammatory response are reflected in the fluctuation of NLR[7]. For the first time, Gunay[8] utilised NLR as a rapid, affordable simple to measure biomarker for the degree of inflammation in COPD patients. The NLR has been shown to be higher among AECOPD patients compared to stable patients and is connected with severity of COPD. Subsequently, numerous studies demonstrated that the NLR was a reliable indicator for COPD exacerbation and mortality. Since there is lack of studies in south India the current study was conducted to analyse the NLR in COPD exacerbation and stable COPD patients.

Aims and Objectives: This study aimed to determine the predictive value of the neutrophil to lymphocyte ratio in patients with stable disease and acute exacerbation of chronic obstructive pulmonary disease.

MATERIALS AND METHODS

Study Setting: Present study was conducted in Department of General Medicine, Sree Mookambika Institute of Medical Sciences, Kulasekharam

Study Design: Prospective cross-sectional study conducted for a period of one year from March 2022 to February 2023.

A total of 80 patients with acute exacerbation of COPD brought to the casualty and stable COPD patients attending the General Medicine OPD were included in the present study.

COPD Exacerbation is defined as the worsening of three or more respiratory symptoms (dyspnoea, sputum, cough, or wheeze) during the course of two or more days. The prerequisites for stable COPD are the absence of exacerbation symptoms and the abstinence from systemic steroids or antibiotics during the previous 8 weeks[9].

Inclusion Criteria: All patients with a confirmed diagnosis of COPD diagnosed with pulmonary function test according to GOLD (Global Initiative for COPD) criteria.

Exclusion Criteria: Patients with bronchial asthma, tuberculosis, history of pulmonary fibrosis, Dementia, receiving systemic corticosteroids, antibiotics, or immunosuppressive treatment and patients not willing to participate in the study.

A thorough history was gathered, including the duration of the illness, smoking history, pack-yearany prior medical conditions. Using the Modified Medical Research Council (MMRC) dyspnoea scale, the degree of dyspnoea was evaluated[10]. Peripheral blood samples were collected from all patients for total WBC count, differential count of neutrophils and lymphocytes and absolute leukocyte values. The test was done in Mindray automatic hematological analyzer in hematology lab. NLR was calculated by dividing absolute neutrophil count by absolute lymphocyte count. Data entered in excel sheet. Statistical Analysis was carried out using SPSS 20.0 version. Significance is assessed at 5% level of significance. One-way ANOVA and Chi-square test was done to assess statistical significance. A p value less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSIONS

In the present study, the age group of patients ranged from 38-68 years of age. Maximum number

Table 1: Distribution of grading of FEV1%

FEV1 %	No of cases
>80% (mild)	10(12.5%)
50 – 79% (moderate)	24 (30%)
30 – 49% (severe)	32 (40%)
< 30% (very severe)	14 (17.5%)

Table 2: comparison of NLR with mean FEV1%

NLR	Mean FEV1 %
0-2.5	71
2.6-5	53.5
5.1-7.5	39.2
7.6-10	29.8

38(47.5%) of cases fell between 61-70 years. Among the patients in the study population 67(83.75%)of patients were males and 13(16.25%)patients were females. The higher prevalence in males is probably due to the higher prevalence of smoking in males.

A significant etiological risk variable for COPD is cigarette smoking. in the current study, all the male participants were smokers, while the female participants were non-smokers. With a p value of less than 0.05, the study found a statistically significant link between smoking and COPD. Among the smokers, 29 cases (36.25%) had consumed 20-29 packs, while 21 cases (26.25%) had consumed 30-39.

In the present study 15(18.75%) had NLR between 0-2.5, 21(26.25%) had NLR between 2.6-5, 35(43.75%) had NLR between 5.1-7.5, 9(11.25%) had NLR between 7.6-10.

According to Modified medical research council scale(MMRC), 28(35%) patients had grade 2 MMRC followed by 23(28.75%) patients had MMRC grade 3 and 13(16.25%) had MMRC grade 4. The scales of NLR and MMRC had a correlation coefficient of 0.025. As a result, the NLR and MMRC scales have a positive connection. NLR rises in parallel with an increase in MMRC grade.

Forced expiratory volume in 1 second (FEV 1%) was done for all patients and was graded as mild, moderate, severe and very severe (Table 1). Table 2 showed that as the mean FEV1% decreases, NLR increases and the comparison showed statistical significance with a p value of 0.001.This demonstrated that the NLR was higher the more severe the airflow limitation (as demonstrated by decliningFEV1).

Among the 80 patients, 62 (77.5%) had stable COPD and the remainder 18 (22.5%) had AECOPD. Another significant finding was that, with a p value of 0.008, the mean NLR was greater (6.981.2) in the COPD exacerbation group compared to the stable COPD group (4.35) in the study. Thus, it may be concluded that NLR can be employed as a predictor of COPD exacerbation.

COPD is a prevalent, preventable treatable condition characterised by chronic respiratory symptoms including airflow limitation. COPD is expected to overtake heart disease as the third largest cause of death globally. COPD was a significant contributor to morbidity and mortality worldwide.11 Lung function, particularly FEV1 is typically used to determine the severity of COPD[12].

Exacerbations of COPD are occasions when the respiratory symptoms get worse, reflecting an aggravation of the existing chronic inflammation of the airways necessitate more therapy. Exacerbations can have bacterial, viral, or other/unspecified causes. Chronic inflammation linked to COPD primarily damages the peripheral airways and lung parenchyma, leading to a mainly irreversible and increasing airflow limitation. An increase in neutrophils, T lymphocytes, alveolar macrophagesinnate lymphoid cells were a hallmark of this inflammation. An elevated neutrophil count in the sputum is linked to chronic expectoration, airway blockagea quick loss in lung function[13].

It is crucial to develop an indicator of prognosis for COPD because its prevalence is rising daily and it is a major cause of mortality. The BODE score, which incorporates body mass index (BMI), dyspnoea scale, degree of obstruction exercise capacity, is a well-known prognostic predictor for COPD[14]. Due to the complexity and impossibility of the BODE score calculation in unwell patients. The NLR has been used in numerous sectors as a developing inflammatory indicator. The NLR may be used to assess acute exacerbations in COPD patients, according to certain research from recent years.

Majority of the patients in the study were in 61 to 70 years of age. The findings of our study are similar to the earlier knowledge since COPD is a disease affecting elderly persons.

In the current study, NLR increases when FEV1% drops, i.e., NLR rises as airflow obstruction severity increases. NLR thus represents the degree of airflow blockage in an indirect manner. Emphysema may develop due to active neutrophils damaging lung tissue by generating oxygen radicals as well as proteolytic enzymes, according to one potential underlying process. The emphysematous alterations can restrict tiny airways. This was comparable to Yasar[15]

According to the current study, the mean NLR was greater in the COPD exacerbation group (6.98±1.2) compared with the stable COPD group (4.35) having a p value of 0.008. A study was conducted on AECOPD patients by Teng[16] According to the study, the NLR was found to be larger at admission (6.89±6.82) than after therapy (4.19±5.11) (P = 0.001).

EmamiArdestani[17] reported that the median values of WBC, CRP, ESR, NLR, as well as PLR were considerably lower in the control group compared to the COPD group (in both AECOPD as well as stable COPD) (p 0.05) in their study on evaluation of the inflammatory markers. Additionally, NLR, ESRCRP levels considerably declined after three months, changing from AECOPD to stable COPD (p<0.05).

CONCLUSION

NLR should be utilised as a regular predictive measure of mortality in all COPD patients because it corresponds favourably with the severity of the disease. The NLR is convenient and reasonably priced to doit can be directly obtained from a routine blood test. The NLR could be gained fast without increasing pain for patients or the workload for clinicians. In an emergency, it can also increase accuracy of clinician when assessing the severity as well as prognosis of AECOPD patients and gives significant support for developing a treatment strategy.

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