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ASSOCIATION OF NEUTROPHIL LYMPHOCYTE RATIO WITH SEVERITY AND OUTCOME OF ACUTE ISCHEMIC STROKE PATIENTS

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***ABSTRACT**--The cumulative incidence of stroke ranged from 105 to 152/100,000 persons per year, and the crude prevalence of stroke ranged from 44.29 to 559/100,000 persons in different parts of the country during the past decade. Stroke is the second leading cause of death worldwide and mostly presents acutely. Among the strokes, ischemic stroke accounts for approximately 80% to 85% of the cases, and is characterized by the disruption of cerebral blood. Acute ischemic stroke is an inflammatory event where the ischemic tissues release chemokines and cytokines, and recruit peripheral circulating leukocytes. Among the leucocytes, neutrophils were found to be an important mediator and early neutrophilia was found to be associated with larger stroke volumes and poor prognosis lymphocytes also infiltrate the ischemic tissues and mediate inflammatory responses neutrophil-lymphocyte ratio as an inflammatory marker has been shown to be associated with poor prognosis in patients with malignancies and acute coronary syndrome.*

***Keywords**--Association, Neutrophil Lymphocyte Ratio, Outcome, Acute Ischemic Stroke*

I. INTRODUCTION

Besides the already known unfavourable prognostic factors in acute ischemic stroke, it is worthwhile to detect new ones and control them at an early stage. Early initiation of treatments for secondary stroke prevention is associated with an 80% reduction in risk of early recurrent stroke.(3) Recent studies suggested that the neutrophil to lymphocyte ratio (NLR) predicts short- and long-term outcome in stroke patients.(4) The main finding of this study is that NLR is an independent predictor of mortality in acute ischemic stroke.(2) A statistically significant increase in mortality caused by stroke was found among patients with higher NLRs.(2) The strong correlation between the NLR, NIHSS score, and GCS score with mortality will support the importance of the clinical course.(2) Low neutrophil count relative to high lymphocyte count at post-AIS should be considered a predictor of a favourable stroke outcome.(5) Conversely, high neutrophil count relative to low lymphocyte count at post-AIS should be considered a predictor of a poor stroke outcome.(5) All stages of cerebral ischemia, but especially acute phase, are associated with inflammatory response.(6) Recent studies showed that neutrophil-to-lymphocyte ratio (NLR) and may be used to assess inflammation in IS.(6) Stroke therapy options have focused on limiting the

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infarct volume. Neutrophil to lymphocyte ratio (NLR) can be valuable to detect the patients that required intensive treatment at early stage by predicting infarct volume.(7-16)

II. OBJECTIVES

To correlate the neutrophil to lymphocyte ratio with severity of acute ischemic stroke and NIHSS scale on admission.

To determine the association of neutrophil to lymphocyte ratio with outcome of patients of acute ischemic stroke measured by Modified Rankin Scale on 30th day of admission

III. METHODS

STUDY SITE

Patients admitted with cerebrovascular event in medicine intensive care unit and medicine wards at the Acharya Vinobha Bhave Rural Hospital.

SAMPLE SIZE

100 patients with acute ischemic stroke admitted in the department of medicine.

TYPE OF STUDY

This will be a Cross-sectional study

INCLUSION CRITERIA

1) Age more than 18 years.
2) Patient with acute ischemic stroke proven by clinical picture, CT scan will be included.

EXCLUSION CRITERIA

1) Patients with an infection history within 2 weeks before stroke.
2) Patients with haematological disorders.
3) Immunosuppressant drug users.
4) Patients with history of malignancy will be excluded.
5) Patients diagnosed with acute haemorrhagic stroke.
6) Patients with recurrent strokes.

IV. METHOD OF COLLECTION OF DATA

The demographics and clinical characteristics of the 100 patients will be obtained from the patient's archive records to evaluate the Glasgow coma score (GCS), national institutes of health stroke scale (NIHSS score) and the Modified Rankin Scale (MRS) at the time of admission and on the 30th day after admission.

V. BLOOD SAMPLE ANALYSIS

A hemogram performed on Pentra XLR Coulter Counter [Five Parts] Hordiba Medical will be evaluated using peripheral venous blood samples taken on admission. NLR will be calculated as the ratio of neutrophils to lymphocytes in peripheral blood. Absolute neutrophil count and absolute lymphocyte count will be calculated manually using a peripheral smear and the NLR value will be calculated as ANC/ALC manually. In an adult, non-geriatric population in good health are between 0.78 and 3.53

Calculation of NLR: ANC/ALC

Interpretation: >3.53-High

<0.78-Low

0.78-3.53-Normal

VI. METHODOLOGY OF CALCULATION OF INFARCT SIZE

CT scan done after admission will be reviewed and in case of acute ischemic stroke, the size of the infarct will be calculated and reported by the radiology department , A.V.B.R.H ., Sawangi , Wardha after applying appropriate computer software .

After all the data is collected the patient will be reviewed on 30th day after admission and the MRS score will be compared with the one that was calculated on admission.

Any increase on decrease in MRS score will be noted and this change will then be correlated with NLR ratio found out on admission.

Sample size and Statistical Analysis

Sample size: A total of 100 individuals will be included in the study.

Sample size calculation

Sample size formula based on prevalence: $N = Z_{1-\alpha/2} *p* (1-P)/ d^2$

Here, Z 1-α/2 is standard normal variate (at 5% type 1 error

Since in the present study P value is considered significant below 0.05 hence 1.96 is used in the equation. P= expected proportion/prevalence in population based in previous studies or pilot study. d= absolute error or precision (0.05) Hence the prevalence of ischaemic strokewill be considered according to International Diabetes Federation Atlas which is 8.8% in India adults So by applying the above formula, when prevalence is 8.8% in the formula

$N = Z_{1-\alpha/2} *p* (1-P) /d^2$ Here, Z=1.96 P=5.59%(From reference cited above)[1] =0.0559 d=Allowable margin of Error=5%=0.05 Therefore; $N = 1.96^2*0.0559*(1-0.0559)/ 0.05^2$=81.05 subjects required in each group Thus 96 = 100 subjects will be taken for study.

STATA version 13 (STATA Corp., College Station, TX) for all data analyses will be used for this study. Continuous variables are summarized by their mean and standard deviation (SD) and categorical variables as crude counts and percentages. Differences in un-weighted proportions between groups will be compared using the chi-square test for independence or Fisher's exact test. All p-values will be significant if <0.05.

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VII. EXPECTED OUTCOMES/RESULTS

The outcome of the research will be discussed after the correlation between NLR and prognosis of AIS is obtained.

VIII. DISCUSSION

The aim of this study is to evaluate the relationship between NLR and infarct volume according to the stroke territory, and to determine the prognostic value of NLR for predicting 3-month mortality in acute ischemic stroke (AIS) patients. After a comprehensive search on PUBMED, the study of NLR is assessment for acute ischemic stroke was found to be carried out in parts of Europe and China and United States. A number of studies in this region on the various aspects related to stroke were reviewed (17-38). Many factors and non-communicable diseases having direct or indirect correlation with stroke (39-57). Few other related studies from this region of Vidarbha were also explored (58-67). In India a study was found on a relatively similar topic by DR. Narra Lavanya et al. Form KIMS Hospital, Bangalore in November 2018.Brain ischemia and trauma elicit robust Inflammation in the brain.(2) Brain cells can produce cytokines and chemokines, and can express adhesion molecules that enable an in situ inflammatory reaction due to the increased expression of adhesion molecules both on cerebral endothelial cells and circulating blood cells.(2) There is accelerated recruitment of leucocytes in the area of ischemia.(2) Neutrophil migration into the damaged area is the first response to ischemic brain damage.(2) Neutrophils are the main source of free oxygen radicals post stroke, which directly destroy the neurons .(2) It has been proposed that baseline neutrophil numbers may be related to tissue damage severity, reinfarct risk, and poor neurologic outcome.(2)

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